Volume IV Nos. 3 and 4

BULLETIN

OF THE

MASSACHUSETTS DEPARTMENT OF MENTAL DISEASES

(PUBLISHED QUARTERLY)

PAPERS IN HONOR OF DR. E. E. SOUTHARD'S DECENNIAL ANNIVERSARY OF THE BULLARD PROFESSORSHIP OF NEUROPATHOLOGY AT HARVARD UNIVERSITY

EDITED UNDER THE PROVISIONS OF ACTS OF 1909, CHAPTER 504, SECTION 6, BY

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OCTOBER, 1920

Publication of this Document
approved by the
Supervisor of Administration.

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INTRODUCTION.

By William N. Bullard, M.D.

It is only very recently that the importance of the study of neuropathology has been at all realized even in the most advanced medical schools of the United States. Up to the beginning of the present century nearly all work of a neuropathological character was done either by physicians who were not specially devoted to pathology, or by general pathologists, very few of whom had any real interest in the study of neuropathological specimens, or cared to devote the time to work in this direction or to learn the difficult and tedious technique required before their results could be of real value.

In the latter part of the last century it was difficult and often impossible to obtain the information desired by the progressive clinician in regard to rare and valuable specimens, and too often the practitioner was informed that a brain or spinal cord appeared "normal" when he knew that his patient had suffered long and severely from symptoms derivable from an affection of these organs. These conditions were not only extremely trying and discouraging to the active practitioner who was desirous to know the pathological conditions of the diseases or affections he was devoting his life to treating, but they also discouraged many men from entering into the study of neurology. It took away from the psychiatrists and the superintendents of the hospitals for the insane and of the sanitaria for those afflicted with mental trouble the stimulus to make themselves, or cause to have made, pathological investigations which would throw light on their problems. Thus many of the superintendents were discouraged from any efforts in this direction, and for this cause among others were driven to devote themselves to administrative rather than to therapeutic or clinical problems.

Hence it seemed very important that some effort should be made to afford to the practitioners of medicine in New England

and elsewhere a definite knowledge of the conditions of the nervous system in their patients, and to study and investigate in general the special pathology of the nervous system, — the brain and the spinal cord and their envelopes and the ganglia and peripheral nerves.

In 1906 the Foundation for a Professorship in Neuropathology was established in the Harvard Medical School by Louisa Norton Bullard in memory of her husband, William Story Bullard of Boston, merchant, and for many years trustee of the McLean Asylum, now known as the McLean Hospital, and situated at Waverley, Mass.

The letter establishing this professorship and accepted by the university was (in part) as follows: —

March 2, 1906.

Bullard Professorship of Neuropathology.

This professorship shall embrace study, research, investigation and teaching in relation to disease of the nervous system whether functional or organic, and shall include not only the affections ordinarily classed under neurology, but all mental diseases and disturbances, both those classed under psychiatry and any others that may exist. The methods and detail of work under this professorship are not restricted. It should include any form of research and investigation which may lead to the increase of knowledge of nervous or mental disease. It comprises the comparative study of these diseases in animals and other living forms.

Since the establishment of this professorship, Dr. Southard has been the only chief, first as instructor, then as assistant professor, and finally as full professor, which he was made in 1909. He was one of the last professorial appointments made during the presidency of Mr. Eliot, and was, at the time he became professor, the youngest professor in the Harvard Medical School.

The whole duty of organizing and administering this Department has since the beginning fallen upon him.

What advances have been made in our knowledge through this Department, and what benefits have accrued to medicine, I shall leave to others to declare.

I cannot leave this subject without expressing the debt that this Department owes to Professor Councilman, professor of pathology, for his constant assistance, advice and interest in all matters concerning its establishment and welfare, and the unselfishness and broad-mindedness shown by him in all relations between this Department and his own.

SUGGESTED LINES OF ADVANCE IN SOLVING THE TYPHOID PROBLEM.

By Frederick P. Gay, M.D.

In a forthcoming monograph the writer has endeavored to trace the development of our scientific knowledge concerning typhoid fever. Numerous treatises of large and small dimension have been written on this important human disease, most of them, however, from a purely clinical aspect, utilizing such scientific information derived from the laboratories as has been immediately of practical value in clinical diagnosis and therapy. On the other hand, various segments of the laboratory aspects of the typhoid problem, for the most part contributed since the discovery of the typhoid bacillus in 1882, have appeared, not only in original articles, but in treatises in connection with textbooks on bacteriology and immunology.

A critical study of the history of the study of the typhoid problem from the dual viewpoints of theory and practice leads to an appreciation of how much the development of the laboratory sciences has meant in clinical medicine. All that we know concerning the exact etiology, and much of our effective knowledge in the epidemiology and modes, of sanitary prevention of typhoid fever rests directly on the discoveries which concern the typhoid bacillus. The only absolute methods of diagnosis depend either on the demonstration of the typhoid bacillus in the body of the patient or on the demonstration of reaction products on the part of the patient to this micro-organism. The prevention of the disease, again, in a specific manner by means of vaccination, of course, presupposes the isolation of pure cultures of the causative agent. Specific therapy in the larger sense of effective or definite therapy would again seem to have depended on recent advances that have been made through discoveries originating in the laboratories.

No human disease offers greater promise of eventual complete disappearance than does typhoid fever, and this disappearance is taking place through the application of the knowledge which we are so rapidly gaining as to the mechanism of this disease, or, more important, as to the life cycle of its parasitic agent within and without the body.

Typhoid fever has disappeared in armies where it was formerly the greatest menace, owing to the extremely suitable age and unusual exposure of those who comprised such aggregations. This disappearance has been due to some extent to improved safeguarding of water supplies, but in great measure to the introduction, first, of voluntary, and later of compulsory, vaccination. The disappearance of typhoid fever, or at least its great diminution in the recent European war, has led to an appreciation of the importance of its hitherto subordinate cogeners, the paratyphoid fevers, and they in turn are yielding to the same type of specific vaccination, as they have been recognized through bacteriological examinations without which their identity would have remained unsuspected. In general communities typhoid fever is still a disease of some importance, more particularly in the country than in the city, where better methods of safeguarding water supplies prevail. Vaccination is by no means a common or recognized procedure as it is in the case of smallpox among the general populations. Of the sources of origin of secondary typhoid cases from original cases of the diseases, the more important are now fully recognized. The typhoid patient himself is no longer a menace under modern supervision. His excreta are properly disposed of and cease to give rise to further cases of the disease. The carrier alone, whether healthy or recovered, remains the most important and still frequently the unexpected source of the disease.

The important lines of advance, in addition to those already undertaken and pursuing their fated course, would, it seems to us, be a special emphasis and recognition of the following factors. First, early diagnosis of every case of typhoid fever, in order that each source of infection may be checked as soon as possible, and in order that the treatment of the patient himself may be as intelligently carried out as may be. This early diagnosis of each case could be brought about by affording the reluctant general practitioner an easy method of obtaining the results from blood cultures. It is suggested that this could be brought about, at least in the larger communities, by an extension of the district nurse system, which would allow a trained technician to take and to diagnose such cultures.

As a second means of combating typhoid fever, it is suggested that every case of the disease should be traced bacteriologically through convalescence to determine the existence of carriers.

It is by no means the rule, even in the best hospitals, for successive stool examinations to be made before discharging a typhoid patient, and yet in no other way can the important group of recovered carriers be detected. There still remain a group of healthy carriers for which the determination of some method of diagnosis more readily available than stool culture is highly desirable. The suggestion is made that the typhoidin skin test should at least be experimented with in this connection.

Most important, perhaps, of all the future advances in respect to typhoid fever will lie in the means of curing carriers once they have been detected. It would seem that certain lines of investigation of a chemotherapeutic nature might be of avail in this connection, particularly in view of the fact that in the rabbit carrier we have an almost perfect analogue to the human condition, which affords at once a ready method of testing the possibilities of any given type of therapy.

Further theoretical studies are desirable to determine the exact nature of the immunity which is afforded by prophylactic typhoid vaccination. This vaccination, although fairly efficient in the majority of individuals for several months, perhaps for as long as two years, fails entirely in certain individuals, and after considerable periods of time in all, to protect against the disease. At all events, it affords by no means so sure a protection as does recovery from the disease. It would be highly desirable to determine the differences in immunity between the two types of protection afforded by recovery on the one hand, and by vaccination on the other. That they are different is suggested by the fact that serum reactions are the rule in the second and less marked type of protection, and are absent, for the most part, in recovered cases after a short interval. The question is open as to whether some new type of vaccine or some modification in the method of administering it would lead to a more enduring immunity than the present methods in vogue. Further testing of the typhoidin test as a means of indicating protection in the individual case is strongly urged.

The intravenous injections of small amounts of typhoid vaccine, or, indeed, of any foreign protein, gives rise to a train of symptoms of a critical nature which is frequently of advantage in aborting or cutting short the course of typhoid fever. The exact mechanism of this beneficial reaction is by no means understood. It comprises an increase in the number of leucocytes,

and its results would to some extent seem dependent on the potency of the antibodies in the patient at the time of injection. Whether the result is due to the upsetting of a ferment, — anti-ferment balance and liberation of the ferment or mobilization of the ferment, thereby destroying the typhoid bacillus in certain parts of the body, — is an open question worthy of further consideration.

A MEDICAL SERVICE WITH THE BRITISH EXPEDITIONARY FORCES IN FRANCE.*

By Ernest T. F. Richards, M.D., St. Paul, Minnesota.

With American troops pouring into France, and American doctors closely following to care for those incapacitated through injury or disease, this is an appropriate time for us to consider some of the problems which our medical colleagues already over there, as well as those who expect shortly to go, will have to meet.

Military medicine differs greatly from civilian, and when one enters an enormous military hospital, such as those now found so numerous in the war zone, one is at once impressed with the fact that he confronts an entirely new realm in medicine. This is probably true of both surgery and medicine, but in medicine in particular one meets with problems dealing not only with totally new clinical syndromes, but with the greater ones of their undiscovered etiology and unguided therapy. It then becomes a matter of learning quickly from first-hand experience how to grapple with such interesting problems as trench fever, gas poisoning, epidemic jaundice, trench feet, shell shock and many others.

This truth — that the gulf between civil and military medicine is vast — was impressed upon me during the winter of 1915 and 1916, when, as the officer in charge of the medical division of a military hospital in France, I welcomed the opportunity to study first-hand in the British Army Medical Service the same problems that the American Army Medical Service is now meeting.

Trench Fever.

Our hospital formed one of a chain of those attached to the British Expeditionary Forces, and was kept filled during that winter with the sick and wounded from the Northern Sector of the British line. One of the most important conditions we met was trench fever. You are all now familiar with the term. Its great importance in military medicine of to-day can not be overestimated. It forms as pressing a problem now as any en-

* Presented before the annual meeting of the Minnesota State Medical Association, Duluth, Aug. 28 to 30, 1918. Reprinted from Minnesota Medicine, February, 1919.

countered in the war zone as, although of itself non-fatal, the morbidity resulting from it on the western front probably exceeds that from any other disease. Those affected with it are in many instances permanently unable to resume their former duties, and some pass back into civil life incapacitated and a charge on the State. The importance of the disease is also emphasized by the fact that in its later stages it is a direct cause of a large percentage of the "irritable heart" of the soldier, of neurasthenia, myalgia, and of so-called "chronic rheumatism" in many of its manifestations. You see, therefore, at a glance how great the need is of most careful study of this condition.

Definition.

Trench fever is now known to be a blood infection communicable from man to man by the louse and possibly other parasites. It may best be defined as a relapsing fever occurring with great frequency among troops on active service, and presenting a uniform group of symptoms which conform with no previously described condition.

Etiology.

Although we now know trench fever is conveyed by lice, the causative organism of the disease yet remains to be discovered. While we were in France every case of fever that came into our wards — and they came in large numbers — was carefully investigated first from the standpoint of etiology. Fortunately our hospital was equipped with an excellent laboratory, so that it was possible to carry out very complete bacteriological studies on all cases. One or two only of the entire number proved to be paratyphoid fever, while not a single case of true typhoid was seen. This is a glowing tribute to the protection afforded by the anti-typhoid and anti-paratyphoid inoculations which every individual — soldiers, nurses, doctors, etc. — is compelled to receive before entering the war zone. So, also, no case of acute rheumatic fever occurred in our entire series — striking evidence against any relationship between this disease and exposure, as practically all of our cases came directly from the trenches where they had been subjected to the most rigorous and changeable climatic conditions. Another interesting fact was that under such conditions acute follicular tonsillitis was extremely rare. True influenza was never proved to occur insomuch as catarrhal symptoms of the upper respiratory tract were

rare, and also careful examinations of sputum and blood cultures were invariably negative for the influenza bacillus.

In those cases of pyrexia clinically diagnosed as trench fever our bacteriological studies, like those of others, were uniformly negative. Such studies included blood cultures, cultures from stools and urine, careful search of fresh and stained blood films, and cultures from muscles and the subperiosteal areas of the long bones.

Though the etiological factor, therefore, in trench fever is yet a matter for speculation, the infectivity of the disease has been proved by Captain McNee of the British Army Medical Corps through its ready transmission from one person to another by means of the blood. This investigator, using healthy soldiers who volunteered for the experiments, found that the disease is transmissible in every case by the whole blood, whether injected intravenously or intramuscularly. He found that blood corpuscles after being washed several times in salt solution to remove the plasma were still infective. Blood corpuscles were broken down and the hemoglobin-tinted fluid passed through a filter in an attempt to prove the virus an ultra-microscopic one confined to the corpuscles. The fluid when injected, however, was not found to be infective.

The report of the British Trench Fever Commission, published last month, has corroborated these findings of McNee's, and has also added further important experimental data. Among these are: That the excreta of infected lice when applied to a broken surface of skin readily produce trench fever; that the bites alone of infected lice do not bring about the disease; that the bodies of infected lice when crushed on the broken skin are capable of producing trench fever; and that the infection is not a disease of normal lice, but, in other words, infection can only be conveyed by lice that have fed upon an individual already infected with the disease.

Clinical Course.

The onset is usually sudden and sometimes is exceedingly abrupt. The patient may suddenly feel giddy with a burning head, he shivers, and may be very short of breath. In such cases of abrupt onset the soldier may have to fall out, if on parade or marching, and often has great difficulty in returning to camp without assistance. He complains of severe headache,

especially frontal and behind the eyes. This is rapidly followed by pain in the lower part of the back, and, on the second or third day, in the legs. With this pain in the legs there is often tenderness on pressure over the shins. The tenderness is most marked over the lower half of the shins, and may be very severe, comparatively little pressure causing the patient to cry out with the pain thus produced. A less degree of tenderness is often present in the calf muscles. The patient generally shivers, but there is never a definite rigor. He is occasionally flushed and often sweats profusely. The appetite is lost. Leucocytosis averaging from 10,000 to 15,000 may be present during the attack. There is no rash.

Depending upon the duration and type of trench fever two clinical forms are recognized: (*a*) the short, and (*b*) the long. In the short form the temperature rises rapidly to between 102 and 104° F. On the third or fourth day the temperature suddenly falls to normal or subnormal, but there is no corresponding improvement in the symptoms. After an interval of a few hours the fever again rises, and then after another two to five days it returns to normal. On this occasion there is immediate relief of all symptoms, and the patient is fit for duty almost at once.

In the long or periodic type, which is the typical relapsing form, the temperature rises to between 101 and 104° on the day of onset. With the fever there are the typical symptoms: frontal headache, conjunctival congestion, shivering, sweating, pain in the lumbar region and in the shins, with tenderness of the shins and calf muscles. After a period varying in length from twenty-four hours to five days the fever drops and all the symptoms disappear. The patient may then be thought to be well and sent back to duty, but after a period of usually five to eight days the fever and other symptoms, especially the pains in the shin, reappear. On this second occasion the febrile period usually lasts about forty-eight hours. It is followed again by a remission and subsequent relapses, or there may be a period of unstable temperature. Eventually a certain percentage of the patients pass into a stage of chronic ill health, suffering from recurrent pains in the limbs, headaches, nervous manifestations such as mental depression, excessive tendency to sweating, disordered action of the heart and abnormal responses to stimuli. The infection, in some cases, is very persistent, and acute febrile relapses may occur after months of quiescence.

Prognosis.

About 90 per cent of trench fever cases yield to symptomatic treatment, and are able to return to duty in four to six weeks. In the remaining 10 per cent the disease pursues a more obstinate course, and may show febrile relapses after periods of several months, or there may be permanent ill health as a result of myocardial irritability, recurring myalgias or nervous exhaustion.

Prophylaxis.

The prophylaxis of trench fever rests upon the extermination of lice. This, under the conditions of modern warfare, is a very difficult problem. To render the men themselves louse-free, the chief measures consist of shaving the hairy parts of the body, hot tubs, and smearing the underclothing with a louse-destroying grease. It might seem that it is not always convenient in trench life to carry out such procedures. However, it is very surprising how quickly the systematic parading of troops from their billets or dugouts, and their thorough disinfestation, has become a part of the modern military régime. The best louse-destroying grease has been the subject of innumerable investigations. At present the most satisfactory grease for application to the underclothing is composed of crude naphthalene, 4 parts, and soft soap, 1 part (Bacot and Copeman).

Clothing, blankets and kits are best disinfected by heat. Dry heat is preferable, as clothing may then be worn immediately after treatment. A temperature of 55° C. for thirty minutes, or 60° for fifteen minutes, is necessary to kill lice and their eggs with certainty. Such temperatures, however, will not disinfect the excreta of lice. The necessary temperatures for this purpose have not yet been determined (Byam *et al.*).

To rid billets, dugouts and huts of lice they are fumigated. The best gases to use for this purpose are sulphur dioxide or hydrocyanic acid gas. The latter is dangerous except in buildings which can be readily ventilated, but it is the more certain of the two (Byam *et al.*).

Finally, in the prophylaxis of trench fever, as in the case of other infections, there figures the problem of carriers. This matter is at present a subject of most careful investigation by the British sanitary authorities. With the disease subject to relapses over indefinite periods of time, the carrier problem is necessarily proving a difficult one to control.

Treatment.

Therapeutic efforts have so far proved unavailing in shortening or modifying to any appreciable degree the course of trench fever. Rest, provided it is begun early enough, followed later with moderate exercise and thyroid therapy, has in the hands of some apparently lowered the subsequent incidence of disordered action of the heart.

The salicylates will in some cases relieve the intense shin pains, but many require morphine. Salvarsan and quinine have proved useless. The sera of convalescent patients have been injected intravenously without influencing the course of the illness.

Of the numerous local applications used for the painful shins, cold compresses of saturated magnesium sulphate solution, first recommended by Capt. D. S. Harvey of the R. A. M. C., seemed in our series to give some relief.

Gas Poisoning.

Turning from this brief sketch of trench fever, let us glance for a moment at what is perhaps the most tragic condition the medical officer in France has to combat, — gas poisoning.

There have been innumerable gases employed in this war. As soon as an antidote is found for one a new gas is invented.

Carbon Monoxide Gas.

Explosives forming CO gas in large quantities when suddenly dissociated are very common in modern warfare. No harm is done by the liberation of this gas in the open air, but in dugouts, caves, mine galleries or deep mine craters, severe and even fatal cases of poisoning occur. The same blood changes, symptoms and treatment apply in these cases as in CO poisoning in civil life.

Drift Gas.

During the winter we spent in France chlorine was the most popular drift gas with the enemy, and "gassed" cases were numerous on our service; during the course of a single night, for example, over 100 victims of this appalling method of warfare were admitted to the medical wards. Chlorine formed an excellent drift gas as, (1) a 1 to 10,000 concentration rapidly puts a man out of action by asphyxiating him, owing to its intense irri-

tative property; (2) it is much heavier than air; (3) it is manufactured in huge quantities in trade processes; (4) it is easily compressible into cylinders for convenience of transport and handling. Moreover, a respirator is easily contrivable to protect the person who manipulates the brigade gas attack, and it is obvious that no drift gas can be used offensively from which the users are unprotected.

Pathology.

The pathological findings in individuals dead of gas poisoning may be summed up as follows: most intense congestion with hemorrhages, edema, and emphysema of the lungs; dilation of the right heart; submucosal hemorrhages of the stomach; and venous congestion of the brain due to the asphyxial character of the death.

Symptoms.

The extent to which an individual is affected by the poisonous fumes differs greatly, and depends largely upon how securely he is able to protect himself with his gas helmet at the time of the attack. The use of these helmets has cut down the mortality rate from gas attacks wonderfully. Both the British and French soldiers place great faith in them as a means of protection, and many of them told us that if they had had their helmets on in time, or if the masks had not been torn, they would have escaped poisoning entirely. In those most seriously affected the picture of suffering presented almost beggars description. The main clinical symptoms may be classified as follows: —

Cyanosis.	Conjunctivitis.
Dyspnea.	Stupor.
Cough with profuse expectoration.	Headache.
Pain in the chest.	Epigastric pain.
Irritation of the throat.	Nausea and vomiting.
Salivation.	Fever.

Physical Findings.

The chief physical findings are, of course, in the lungs. Difficult rapid respiration and pain upon breathing are prominent. Over both lungs, and most marked over the lower lobes, there is impaired resonance ranging from slight to well-marked dullness. Throughout the chest, frequently obscuring the heart tones, harshened breath sounds accompanied by râles of every

known variety are the prominent findings upon auscultation. Especially notable is the coarse, bubbling type of râle situated at the lung bases. In about 2 per cent of our cases bronchopneumonic patches of consolidation appeared at the end of the first week of illness. In one case of the series a large serous exudate occurred in the pleural cavity in the fourth week.

Feeble heart tones, increased pulse rates, low blood pressures, and occasional definite myocardial dilations are the chief circulatory phenomena.

Other physical findings are: evidences of laryngeal irritation; cyanosis; heavily coated tongue, often of a greenish yellow color; foul breath; tenderness in the upper abdomen, being in some patients very marked; and, depending upon the depth of the stupor, diminished pupillary, skin and deep reflexes.

Course of Illness.

In the majority of our cases, even in those classified as mild, both physical signs and symptoms were very slow in clearing up. This was especially true of the cyanosis, which showed great tardiness in disappearing and a marked tendency to return upon slight exertion, such as sitting up in bed, even when all other evidences of poisoning had gone.

Dizziness was another obstinate symptom, and often while not present while lying in bed was frequently very troublesome during convalescence when attempts were being made to get the patient up and around. In several cases, owing to the dizziness, confinement to bed was necessary during the entire stay in the hospital, which extended sometimes to five and six weeks, after which, if not sufficiently well to be transferred to a convalescent camp, the patients were sent to England by hospital ship.

Cough and expectoration were also slow in improving, and persisted in many cases well into convalescence.

Fever of slight or moderate degree lasted in the most severely ill throughout their entire stay in hospital.

Convalescence, even in mild cases, was slow, and attended with considerable muscular and nervous exhaustion. Several patients, after a five weeks' stay in bed, had to be shipped on stretchers to England to convalesce. Recurrence of cyanosis and dizziness on exertion, coupled with a low blood pressure, an accelerated pulse and anemia, frequently made their further convalescence exceedingly tedious.

Treatment.

The treatment adopted by us for this distressing condition consisted of —

Enforced rest in bed.	Oxygen inhalations.
Fresh air.	Venesection.
Forced nourishment.	Atropine sulphate.
Expectorants.	Strychnine, digitalis and morphine.

It is somewhat problematical which of these measures were of the greatest moment, but with a large number of the cases desperately ill on admission, the total mortality rate under this régime was only 3.5 per cent.

Rest in bed with the maximum amount of fresh air, the patient being kept as warm as possible, and forcing of nourishment, were undoubtedly important factors in saving the lives of many.

Of the expectorants, ammonium carbonate used early helps to clear up the copious frothy sputum.

Inhalations of oxygen strikingly relieve the air hunger, the cyanosis and the distressing dyspnea. In those most seriously ill it was freely used at short intervals, the patients themselves frequently begging for it. When possible the patient should be kept in an atmosphere of pure oxygen until all alarming phenomena have disappeared, even if this requires a continuation of the oxygen supply for several days.

A most important measure is venesection. In those cases showing extreme cyanosis, greatly labored breathing or right heart dilation venesection was employed with very great benefit. It was followed in each instance by a distinct lessening of the cyanosis, diminution of the headache, and improvement in the other symptoms. From our observations it would appear that this measure, to be of most value, should be carried out early and repeated, if necessary, at rather frequent intervals, with the withdrawal of only moderate amounts of blood on each occasion.

Atropine sulphate, in large doses hypodermatically, was of definite value. Strychnine was of doubtful, but in a few instances of some apparent, value. Tonic doses of digitalis, after the acute stages of the poisoning had subsided, and particularly during convalescence, was distinctly beneficial.

Shell Gases.

At the present writing drift gases have been largely replaced on the western front by shells containing chemicals in liquid form generating toxic gases in the presence of moisture. Dichlorethylsulphide, better known on account of its odor as mustard gas, has been extensively used by the Germans since they first employed it against the British troops in July, 1917. When such a shell strikes an object a special fuse explodes a chamber of picric acid, bursts the shell, and sprinkles the liquid over a large area.

Since November, 1917, a new chemical has been identified in German shells. This substance, commonly called arsine, is diphenylarsine-chloride. As found in the clothing of gassed men, it consists of fine solid particles having a strong garlicky odor (de Tarnowsky).

In both mustard gas and arsine the symptoms are: severe epigastric pain accompanied by repeated emesis; coryza of varying severity; conjunctivitis with profuse lacrimation, and, in some cases, photophobia; cutaneous symptoms, such as, erythema, severe itching, blisters and edema. After two to three days a painful laryngitis, often with aphonia, followed by severe bronchitis, develops.

The shell gases have been most successfully met by the British and French medical men, and the mortality rate has been very low. The most important means of protection are the gas masks provided with the proper antidotes (which obviously for military reasons cannot be discussed at this time). The general management of these gases is similar to that described for chlorine poisoning. Gastro-intestinal symptoms are fairly well controlled by the daily administration of 100 cubic centimeters of a 1 to 1,000 solution of saccharate of lime. For the eyes, sodium bicarbonate washes give relief. For the respiratory tract the application, by means of an atomizer, of a protective oily solution such as liquid albolene gives excellent results in the milder cases; for the severe cases intratracheal sprays are employed. For the skin lesions the British employ douches, bathing and wet dressings of sodium bicarbonate solutions; the French treat all their burns with a protective dressing of gutta-percha (6 to 10 per cent) and paraffin (90 to 94 per cent), made popular under the name of umbrine.

Infectious Jaundice.

Infectious jaundice, another important medical problem occurring among the troops in France, was of especial interest because of its striking similarity to the infectious jaundice seen in civil practice. The condition is substantially the same as that described in 1886 by Weil, and since known as Weil's disease. As is well known, widespread epidemics of this condition have been recorded in the United States. Its chief features are: jaundice, fever, hemorrhages, and the occurrence of cases in epidemics or localized groups. The Japanese worker, Inada, and his collaborators have established from a study of the disease appearing in Japan that the infection is caused by a spirochete, — the spirocheta ictero-hemorrhagica. The organism appears to gain access to the human individual through the alimentary canal, and possibly, also, through the skin. Lice have been considered as possible intermediate hosts, but the tendency now is to blame the field rat, as Inada and his coworkers have succeeded in finding the spirochetæ of jaundice in the kidneys and urine of 38 per cent of ordinary field rats in the infected areas in Japan.

That it is possible that other organisms, such as the *B. paratyphosus*, may be factors in the production of epidemic jaundice must be kept in mind, but it would appear that the great majority of cases of infectious jaundice met with in armies on campaign can be accepted as examples of Weil's disease.

The clinical course of the infection as we observed it in France was of a fairly uniform type. The onset may be abrupt with a chill; or more gradual with intense headache, dizziness, nausea, persistent vomiting, diarrhœa and abdominal pain. An irregular fever develops, and jaundice appears in forty-eight to seventy-two hours, at times of but slight degree, but gradually deepening in the severe cases. Hemorrhages into the skin and conjunctiva may take place. Bleeding from the nose, mouth, stomach or bowels may occur in the severely jaundiced cases. A decided albuminuria with numerous casts and red blood cells is a striking feature. In the severe cases the prostration is practically a collapse. The muscular soreness prevents movement. The legs may be swollen. Active delirium may be present. Drowsiness with slowness of the pulse is common. After three or four days, in a mild case, the fever gradually

drops, convalescence slowly begins, and the yellow color gradually fades. Slight or severe febrile relapses may occur, or a mild fever may continue for twelve to twenty days. In a fatal case the jaundice deepens, vomiting is marked, the temperature becomes subnormal, prostration is extreme, and the patient dies of exhaustion. Physically, jaundice of greater or less degree, with injection of the conjunctivæ, herpes, dry tongue, sordes, and late-appearing papular rashes in a severely prostrated patient, make the general picture of the disease. The abdomen is usually tender, and resistant if the pain is extreme. The liver and spleen are usually not enlarged.

The prognosis may be said to be favorable, even in the more severe cases. The death rate averages less than 6 per cent. The virulence of the disease as seen by us in France is much less than that described in Japan.

The treatment of infectious jaundice is at present purely symptomatic. Good nursing, unlimited fluids, fresh fruits, and the rectal administration of glucose (6 per cent solution, 1 pint) once or twice daily in cases with vomiting and acetonuria, are the main indications.

Many other conditions, as, for example, shell shock, trench feet and trench nephritis, make, together with those we have discussed, an active medical service in a military hospital a rich and treasured experience. But apart from this and the valued associations one makes, to the doctors who serve comes the greatest recompense of all, — the conviction that they form an absolutely essential and indispensable factor in winning the greatest war ever fought for the sake of humanity.

MOTION STUDY OF INOCULATING TUBES.*

By M. M. Canavan, M.D., Boston,

assistant pathologist, massachusetts commission on mental diseases; formerly pathologist, boston state hospital.

A standard method of inoculating culture tubes is presented with picture showing details of arranging and placing the apparatus and the movements of the operator in inoculating tubes.

The major portion of the writer's technical bacteriological practice was performed at the Danvers State Hospital Laboratory under the direction of E. E. Southard, who was then (1906 to 1909) pathologist to the hospital. During that time extensive bacteriological research was done in post-mortem bacteriology,[1,2,3,4,] epidemic dysentery,[5] endemic dysentery[6,7] and diphtheria.

This method was gradually and unconsciously evolved from pressure of work: Technique will occur to any one performing the same operation over and over in which the muscles gain an automaticity and mechanically assist the operator by traversing their paths, leaving the mind free for emergency or supervision, and would probably have been as unconsciously forgotten had not a "scientific selection" of a place for a summer vacation been made as a result of hearing Mr. F. B. Gilbreth read his paper on "Motion Models as a Method of Education" before the section on education at the American Association for the Advancement of Science, in Columbus, 1915. Mr. Gilbreth invited the section to attend the summer school in Providence, and at this time (1916) micromotion studies of mechanical movements were made. An accurate study of the process here presented was pictured. Mr. Gilbreth commented favorably on the results,[8] which showed an average time of twenty-four seconds.

Apparatus.

With a clear flat space 28 by 16 inches, a Bunsen burner, gas connection, matches, tubes of mother culture, empty wire baskets, a platinum loop, a sharpened pencil, sterile tubes of culture media, a small block for slanting one basket, a table or

* This is one of a series of fifteen papers (261, 1919.4) offered to Prof. E. E. Southard in honor of the decennium of the Bullard Professorship of Neuropathology, Harvard Medical School. Reprinted from the Boston Medical and Surgical Journal, Vol. CLXXXIII, No. 4, July 22, 1920, pp. 103-105.

desk at appropriate height with chair to accommodate the operator, one can rapidly reproduce the setting for this work.

By following the picture from left to right, the process and angle of holding tubes, the order of assembling, etc., are perfectly seen.

The gas burner, at full height of flame, is in the center directly in front of the operator, as are also the mother tubes in an ordinary glass tumbler. This differentiates them for all time, and prevents mixing them with the sterile culture tubes (on the right in baskets) and with the freshly inoculated tubes on the left (slanting basket).

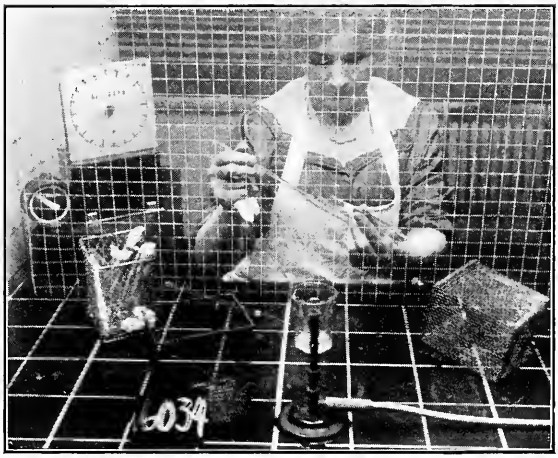
Between the center and the culture tubes on the right is an empty wire basket on top of which rests the platinum wire loop, No. 20 gauge, fitted into a glass handle; this placing prevents it from rolling into the operator's lap or taking other excursions calculated to delay the proceedings, and it is near the height of the flame in which it is necessary to pause; also a pencil lies on the table in this sector, and a matchbox is at the base of the burner. To the left is a basket placed in a slanting manner with its opening toward the center of the semicircle of the field of operation.

The Cycle of Motion.

The cycle of motion consists in placing the mother tube in the left hand between the thumb and index finger, resting the free edge against the partly flexed second finger.

Next select a sterile tube with the right hand, to lie parallel to this tube; twists are rapidly made of cotton plugs to make sure that they are free from the sides and are of proper snugness. Then the right hand picks up the glass rod, "flames" it by holding it perpendicularly to the gas flame and in it until the wire has a dull red glow, then passes it horizontally through the flame twice to rapidly sterilize without breaking the glass connection.

The next step consists of moving the left hand holding the tubes to the palm of the right hand, the little finger of which closes over the cotton in the tubes and holds the plugs firmly against the palm of the hand, at which time the left hand is separated from the right hand and the plugs are left firmly held away from possible contamination in the palm of the right hand, the thumb and forefinger of which support the loop which is cooling, since a red-hot rod while sterile would cause great



Set-up showing position of apparatus on 4-inch blocked table, with slant of needle and tubes shown by 1-inch screen.

devastation of bacteria in the mother tube. The left hand approaches the open tubes to the flame, sterilizing their throats. The right hand holding the platinum loop seeks a safe space behind the flame as the left hand pulls back the tubes and the platinum loop moves into the throat of the mother tube and gently rakes up some of the bacteria which is on the surface of solid media or which is caught up from the fluid media, and with a slight turn of the left hand from the wrist, while the loop is withdrawn from the mother tube, the second tube is in position for the transfer of the culture, and the throat of the sterile tube is entered and the bacteria deposited in the medium.

The tubes are again flamed, the stoppers replaced by one movement of the right and left hand reversing the withdrawal of the cotton. The right hand sterilizes the loop and lays the rod down over the top of the wire basket, swooping to the top of the table to pick up the pencil with which to write on the label the pertinent facts, after which a new culture tube is placed in the slanting basket to the left and a fresh tube is selected to begin a new cycle.

Advantages of this Method.

1. Semicircular setting of apparatus conducive to greatest convenience.
2. Bare forearms prevent tipping by coat sleeves or cuffs.
3. Elevation of platinum loop prevents its becoming misplaced, and gives easy grasp.
4. *Pulling two cotton plugs by one movement and replacing by one movement* made possible by uniform distance between the tubes.

What studying a Method by Micromotion teaches the Operator.

1. Necessity for having apparatus well arranged.
2. Desirability of maintaining standard conditions.
3. Incentive to improvement in technique.
4. Confidence in method.

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8. Boston Sunday Post, Aug. 27, 1916.

ACUTE CHANGES OCCURRING IN THE CELLS OF THE SOLAR PLEXUS IN INTESTINAL CONDITIONS.*

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In some previous papers I described chronic pathological changes taking place in the sympathetic nerve cells of the solar plexus of insane patients and described some acute changes as well. The following two cases in which acute intestinal conditions occurred were associated with acute changes of the nerve cells of the type described as acute Nissl degeneration. The relationship of the sympathetic nerve system to intestinal conditions has been very insufficiently studied, and, in part, this is the reason for presenting these two cases.

Case 1. — White woman, No. 16344, autopsy No. 152. Entered the hospital April 1, 1904, age, 42. The diagnosis of dementia præcox, catatonic and paranoid, rested on the following mental symptoms: Delusions of persecution, poisoning, and of reference; markedly negativistic; hallucinations of hearing; increasing dementia. She died April 14, 1916. Unfortunately, she had been for so long a time in a highly negativistic, semi-stuporous state that no change was noted until just before death, when the distention of the abdomen became marked. Autopsy held eighteen hours later. Summary of gross findings: emaciation, poor development; small heart, 180 grams; small aorta; lungs, chronic passive congestion; atrophy of spleen, liver, pancreas and kidneys was marked; atrophy of ovaries and uterus; no arteriosclerosis anywhere.

Brain. — Few adhesions of dura; pia not remarkable; brain firm; section negative, except for slight congestion; weight of brain, 1,150 grams; spinal cord negative; pituitary negative.

Abdomen. — Volvulus was found of somewhat unusual character. The ascending colon had a long mesentery which had become twisted so that this portion of the gut was thrown over to the left side and the small intestines had looped themselves around the stalk in an intricate manner. The ascending colon was distended, deep red generally, and deep blackish red in places. There was no break anywhere noted. The small intestines were distended. Peritoneum and mesentery much injected and moist. Scattered small hemorrhages.

Cause of Death. — Volvulus. Passive congestion of lungs.

* From the Pathological Laboratory of Taunton State Hospital. Reprinted from the Boston Medical and Surgical Journal, Vol. CLXXX, No. 8, pp. 207–209, Feb. 20, 1919.

Microscopic Examination. — The main interest centers on the nervous system, since there was nothing of unusual character in the body organs. In general, the macroscopic examination was confirmed.

Brain shows chronic changes often found after middle life and accompanying emaciation. Whether they are related to dementia præcox is not at all certain. There is atrophy of the nerve cells, especially the deeper layers; very slight satellitosis; lipochrome granules in the large nerve cells. Very occasionally a cell showing acute changes with diffuse Nissl staining and eccentric nucleus noted.

Sympathetic cells of solar plexus. Cells here show two types of change. First, a chronic type, characterized in the previous paper before mentioned as belonging to "neurathrepsia." There is increase of the capsular cells, with atrophy of nerve cells, marked pigmentation, which on analysis are lipochrome granules, eosinophilic granules, and by silver staining after the fat is removed, the black or argyrophilic granules. Second, acute changes of typical axonal nature are present. There is almost complete disappearance of the Nissl bodies, only the fringe of the cell staining a diffuse blue. The nucleus in the majority of cases is in the very periphery of the cell, and in certain cases has been completely extruded.

In striking contrast to the changes found in this ganglion is the condition presented by the Gasserian ganglion which, of course, represents anatomically and functionally a different type of ganglion. Here the cells show typical normal Nissl staining, and the nuclei are central. Though there are some chronic changes presented, nothing of acute nature has occurred.

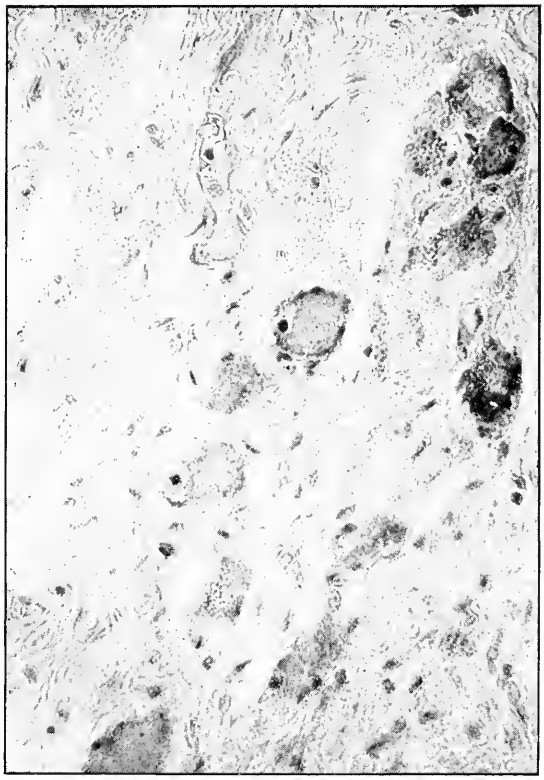
Summary of Case. — A dementia præcox patient, woman of middle life, dying of volvulus, shows acute axonal reaction in the sympathetic cells of the solar plexus, without corresponding changes elsewhere.

Case 2. No. 20085, autopsy No. 146. Entered hospital April 22, 1912, 20 years of age; died March 26, 1916.

Summary of Clinical History. — Always backward; enuresis until the age of 15; active mental symptoms at 18. Physical examination at the time of entrance showed exaggerated tendon reflexes, ankle clonus; unsteady gait. Positive Wassermann reaction in blood. Spinal fluid: puncture attempted and unsuccessful because of patient's intense excitement and resistance. Mentally, patient is excited and grandiose. Gradually deteriorated, became apathetic and deeply demented — bedridden. She died on date mentioned. Had, clinically, signs that pointed to the consolidation of left lung.

Summary of Autopsy Findings. — Marked emaciation. Left lung is pushed upward and occupies only the upper part of the chest. Rest of pleural cavity occupied by serous fluid; no pus, no fibrin. There are a few scars, moderately calcified, in the thickened pleura of the apex. The lung is not solid.

Aortitis. Moderate myocarditis. Atrophy of spleen. Hepatitis. Cystic ovary.



Brain. — Typical well advanced general paresis; that is, thickened dura, cloudy and adherent pia, atrophy of convolutions in frontal and parietal portion with increased firmness, granulations in fourth ventricle, increased cerebrospinal fluid, etc. Cord shows moderate changes in posterior columns.

The large bowel and part of the ileum were distended with impacted feces. The blood vessels of the peritoneum were distended and engorged.

Microscopic Examination. — Lung shows congestion, compression, polymorphous and endothelial leukocytes in alveoli, no fibrin, occasional giant cell seen in thickened pleura. Brain: typical paresis. Perivascular spaces filled with lymphocytes and plasma cells. Pia thickened and contains exudate. Nerve cells show disarrangement of layers, atrophy, vacuolization. Diffuse Nissl staining. Central nuclei. Red cells present. Increased capillaries, increased neuroglia cells.

Sympathetic. — Very decided acute changes in nerve cells with only a slight fringe of methylene preceding cases; that is, there is pallor of the nerve cells with only a slight fringe of methylene blue staining material at the periphery. The nucleus is peripheral, and it shows varying degrees of extrusion. The chronic changes so well marked in the previous case are not nearly so prominent in this section; pigmentation is less marked.

Summary. — A juvenile paretic, dying of pleurisy with effusion of tubercular origin, fecal impaction and congestion of peritoneal blood vessels, shows acute axonal reaction in the sympathetic cells of the solar plexus.

Discussion.

The pathological condition here reported as occurring in insane patients is not at all related to the mental conditions of the patients, since in neither paresis nor dementia præcox, as these conditions come to the autopsy table, can it be found. This statement is based on routine study of over 100 cases. Nor can it be related to tuberculosis, which is the cause of death in the second case, for it is not present in other tubercular cases. Emaciation itself plays no part, for many of the patients who are autopsied in insane hospitals are emaciated, dying, as they do, of chronic diseases and often refusing nourishment. While it is impossible on the basis of two cases to make any conclusions regarding the phenomenon, a tentative relationship may be discussed. It is very possible that pathological conditions that affect the blood supply of the ganglion are responsible for the acute changes described. It is well known that the ligature of blood vessels leading to other parts of the nervous system produces such changes. The volvulus has its main effects through this change in blood supply, and it is conceivable that fecal impaction would disturb the circulation of the abdomen

enough to produce anæmia or congestion to the nerve cells of the ganglion. If this be so, it is very likely that part of the collapse and shock noted in such conditions as volvulus, intussusception, and acute intestinal obstruction of any kind may be related to the changes in the nerve cells of the solar plexus. A disturbance created in the center which controls so many viscera and plays so large a part in blood vessel control may well be general in symptomatology.

Speculation becomes somewhat more precarious in passing from these acute conditions to chronic disturbance in the abdomen. Chronic congestion of the peritoneal vessels such as occurs with adhesions, obstipation, cirrhosis of the liver, etc., should be studied from the viewpoint here tentatively advanced. Mechanical and nutritive changes acting on the sympathetic cells of the abdomen rather than any auto-intoxication may account for the generalized symptomatology.

Here, too, it is possible that one may find an explanation of the change in mood, so often immediately noted after an evacuation of the bowels. The change produced is almost instantaneous with many people. Mood and emotion are largely vaso-visceral manifestations, and it seems to me likely that a loaded bowel changes conditions within the intestine in such a manner as to affect the blood supply of the sympathetic cells scattered in the ganglia throughout the posterior wall of the abdomen. That not all people are bothered by a loaded bowel may be explained by some difference in the architecture of the peritoneum, in the length of the attachments, any difference in the ligaments; in other words, it may be related to mechanical differences, so that congestion and vascular disturbances may much more easily be produced in certain individuals than in others.

A COMPARISON OF THE ANTERIOR HORN CELLS IN THE NORMAL SPINAL CORD AND AFTER AMPUTATION.*

By A. E. Taft, M.D., Philadelphia,

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This work arose from the negative results of an examination, by a student in the department of neuropathology, of three spinal cords from cases having had amputation of a limb some time previous to death. The findings were so little in accord with the idea of post-amputation pathology gained from various textbooks that a further examination of cords was undertaken in the same manner from subjects not showing signs of cord lesions during life, and from that point of view called normal. Except for this general precaution material was chosen at random.

A variety of findings are recorded in the literature as a result of investigations of the changes in the anterior horn cells following amputation. No attempt has been made to include a complete literary review; the plan is only to give an idea of the varied results arrived at by a number of experienced investigators.

Literature.

Campbell [1] says, after considerable work on this subject, "it may be explained that in consequence of such a lesion alterations occur in the spinal cord, and these in time occasion striking and characteristic appearances. In long-standing cases the predominant change is a homolateral atrophy, represented by a general reduction in volume of white and gray matter alike, and involving those particular segments of the cord which receive and give off the sensory and motor nerves which originally supplied the skin and muscles of the amputated member. Wasting of the gray substance is accompanied by the numerical reduction of its contained nerve cells, both large and small, and while all the cell collections in the anterior cornu suffer, one special group may be singled out as being specially prone to atrophy, namely, the posterolateral."

* Contribution in a series offered to Prof. E. E. Southard in honor of the decennium of the Bullard Professorship of Neuropathology, Harvard Medical School.

Marinesco,[2] one of the earlier investigators of this question, is one very often quoted. His report includes three cases: one with duration of twenty-one years; one ten years; and the third of unknown duration. He found changes in anterior horn cells: in the first two cases a reduction in number on the side of the amputation, not only in the lateral, but in other groups; in the third case neither the cell count in the posterolateral group nor of all cells in all groups have sufficient significance to conclude that there is any definite change in the cells.

Edinger [3] reports a case of prenatal amputation of the left lower arm with death at fifty-two years of age. The left side of the cord corresponding to the four lower cervical and first two dorsal segments showed a distinct atrophy of the anterior horn, which was greatest at the level of the sixth and seventh cervical segments. There was also a distinct decrease in the size and number of the anterior horn cells, especially at the anterolateral and posterolateral angles of the anterior horn. In three additional cases of post-amputation, no convincing proof of cell atrophy was found in the anterior horns.

Van Gehuchten [4] examined the lumbosacral cord from a case twelve years after amputation of the lower extremity in the middle portion of the thigh. The anterior horn cells representing the foot muscles were normal, while the cells representing the muscles below the knee had disappeared in spite of the fact that the axons of both groups of cells had been divided.

Déjerine and Mayer [5] studied eight cases of amputation varying from four to forty years following amputation. They found in all cases a definite decrease in the size of the side of the cord corresponding to the amputation, affecting both white and gray matter, both anterior and posterior. In only one case were histologic changes found; this was following amputation of the thigh, of thirty years' duration. In the middle of the lumbar enlargement a definite decrease in the number of anterior horn cells appeared, the number being only a third of the normal side, and the anteromesial group was the one most affected.

Elders,[6] in an excellent article, reports the examination of the cord of a person born without the left lower arm. Death occurred at fifty-four years of age. In the lower half of the left cervical segment the posterolateral angle was rounder and shorter than the right, and contained fewer cells.

Dreschfeld [7] examined a case of amputation of the left thigh fifteen years after operation, and found atrophy of the anterior

horn and some change in the posterior horn in the lower part of the left lumbar enlargement, with decrease in number and atrophy of the nerve cells of the intermediolateral group.

Kahler and Pick [8] report two cases, one of which was an amputation of the lower third of the left thigh eighteen years after operation. The anterior horn cells were decreased in the anterior group. The second case was an amputation of the left forearm in the lower third. He reports partial atrophy and decrease in the number of cells in the lateral group.

Dickinson [9] reports findings on a case of amputation of the right leg fifteen years before death, in which there was a decrease in the number and size of the nerve cells of the corresponding side.

Genzmer [10] found decrease in size of anterior horn and in the number of anterior horn cells on the amputated side in a case of amputation of the lower third of the right thigh thirty years before death.

Hayem [11] examined the cord in the case of exarticulation of the wrist five years after operation, and found general atrophy of the anterior horn with atrophy of nerve cells, most marked at the level of the eighth cervical and first dorsal nerves.

Friedreich's [12] case of amputation of the left forearm twelve years before death showed no changes in the cord; the anterior horn cells were intact.

Animal Experiment.

Experimental work also has been done on various laboratory animals, both by section of nerve trunks and by amputation of extremities.

Van Gehuchten [4] divided the sciatic nerve and later found only the cells of the posterolateral group affected.

Homen's [13] work on animals showed a slight atrophy and decrease in the number of cells of the anterior horn. The individual cells were found in general somewhat smaller than the corresponding ones, on the opposite side. No changes were found in the brain.

The experimental work of Warrington [14] is a more recent and detailed investigation of the changes of the anterior horn cells after section of the spinal nerve roots. In some instances changes were found both in anterior and posterior horn cells corresponding to the side operated on. He reports finding changes not only on the corresponding side, but also on the

opposite side. "After section of several posterior roots from the VIth to the IXth post thoracic, inclusive, a considerable percentage of obviously altered cells are found. Their distribution in the case of the cat is practically limited to the VIIth and VIIIth segments, and especially to the posterolateral group of cells in those segments. In the monkey the upper part of the VIIth segment is picked out. The effect is to a very slight extent a crossed one, and presents the remarkable feature that more affected cells were found in the VIth segment of the crossed side than on the side of the lesion." Further, "The view I wish to maintain is that the changes are the result of the withdrawal of the afferent impulses which normally impinge on cornual cells. Histological evidence shows that the posteroexternal group of anterior horn cells is most richly innervated by the collaterals from the posterior roots." He thus explains the degeneration of this group of cells, and adds further, with emphasis, that the changes occurring after section of the posterior roots are much more intense, and that the ultimate destruction of these cells is more likely to occur than after the division of the anterior roots alone. After section of both anterior and posterior roots all the larger cells on the side of the lesion showed changes. The greater number were only slightly affected compared to the extent seen after section of an anterior nerve root alone; others, however, showed a much more marked chromatolysis, the changes resembling those found after section of the afferent roots. He finally concludes that there is a tendency for the altered cells to return to their normal structure regardless of the regeneration of their axons, in conformity with the opinions of Van Gehuchten and Nissl.[15]

From Textbooks.

Concerning the change in the anterior horn cells following division of their fibers Oppenheim [16] says: "The Nissl stain shows destruction of the granules and an excentric position of the nucleus. If a restitution in the periphery takes place, regeneration results. If, however, there is no peripheral regeneration, further change in the form of atrophy takes place in the cells."

Van Gehuchten: The section of the axon leads to a rapid swelling of the cell protoplasm, and consequent displacement of the nucleus. He believes that in a small number of cases the swelling of the cell body takes place so rapidly, and the force which pushes the nucleus to one side is so powerful, that it is

driven completely out of the cell body. These cells are the only ones, he concludes, which completely atrophy, while all the others slowly return to normal.

Déjerine and Thomas:[17] For localization studies, division of nerves has been made. In man, the cords of persons having had amputations have been studied with the same end in view, but the application of this method has not always been free from reproach.

Schafer: If the degeneration has been caused by section of the axon, the reparative process is very slow, so that it may be three or four months before it is completed. At the end of this time the nerve-cell bodies have resumed their original appearance even though reparation of the cut nerve may be incomplete.

Barker:[18] The motor fibers of the central stump gradually diminish in number; in some instances they appear to vanish almost totally, and a large number of the motor cells of the ventral horns dwindle in size, and after a time actually may be lost.

Material examined.

The tissue was prepared in serial paraffin sections, 6 microns thick, and stained by the cresylechtviolet cell-stain method.

Material from three cases of amputation was examined as a starting point of this work, and mainly from the point of view of loss of anterior horn cells. Sections were examined from the segments of the cord corresponding to the part amputated, and the cells of both anterior horns were counted.

Case 1. — Man, aged 79, sixty years after amputation of left arm. The anterior horn cells showed no chromatolysis, but many of the cells were well filled with lipochrome. This is not unusual in view of the age of the man. One hundred and thirty-three serial sections were counted. The variation in individual sections was considerable, but the final average of all counts was, right 17, left 19, or an average of two cells more on the amputated than on the opposite side.

In the brain the Betz cells and other large elements contained much lipochrome, but showed no reaction to the amputation.

Case 2. — Man, aged 65 years, recent amputation of lower third of the left leg. The anterior horn cells were very little altered. There was no chromatolysis, and very little lipochrome. Forty-one serial sections were counted. Variation in individual sections was as much as 62: 38 between the two sides. The average of the total number counted was, right 52, left 55, or an average of three more cells on the amputated side. As the operation in this case was performed only the day before death

(following gangrene of the foot), no permanent change in nerve cells would be expected. No axonal change had taken place.

Case 3. — Female, aged 73, old amputation of right thigh. The anterior horn cells contained a great deal of lipochrome, but also some normal Nissl granules. A total of 41 counts was made on serial sections. The variation in individual sections was as great as 13:32. The total average was, right 21.8, left 23.9, or an average of two more cells on the non-amputated than on the amputated side.

In addition to these counts others were made on material from a variety of cases, with the single precaution that they show no clinical signs of cord involvement. Both sexes were included, and the ages ranged from eleven months to seventy-one years.

One case, considered particularly suitable for use as a normal control, was that of a young male adult, thirty-seven years of age. Here the average of 67 counts in the cervical region was 50 on one side and 54 on the other; of 53 counts in the dorsal region, 12.0 on one side and 12.9 on the other; in the lumbar region the average of 62 counts was 49.5 on one side and 52.0 on the other. This variation is seen to be greater than in the cases of amputation. In Marinesco's [2] work the greatest number of sections of one level counted is 16, and the variation in the sum total is 245:223. In the instances where a smaller number of sections were counted, the difference between the two sides was even greater. In the case of the normal control just described, in one group of 21 counts, the total was 938 on one side and 1,181 on the other; but in the final sum of all counts, 67 in all, the number was 2,603 on one side and 2,684 on the other.

In the accompanying table the detail of the entire number of cases counted may be seen. No attempt was made to identify the exact segment of the cord from which the blocks were taken, as much of the material was already embedded without regard to this detail; consequently, there is a great difference in the count at the varying levels. It may be noted also that numbers are much larger up to and including Case 26 than in the subsequent ones. This is due to the fact that in the earlier cases all cells were counted which represented the full contour of a cell including any of its processes, exclusive of whether it contained a nucleus or not. Later, only those cells were counted which contained a stained nucleus. But since the comparison is that of the two sides of the cord, and not between different specimens, the relation is not altered.

TABLE SHOWING COUNTS OF ANTERIOR HORN CELLS IN SERIAL SECTIONS OF SPINAL CORD.

Following Amputation.

Case.	Diagnosis.	Sex.	Age.	Cervical.		Dorsal.		Lumbar.		Sections counted.
				1.	2.	1.	2.	1.	2.	
1	Amputation, left arm.	M	79	19.3	17.4	–	–	–	–	133
2	Amputation, left leg.	M	65	–	–	–	–	55.	52.	41
3	Amputation, right leg.	F	73	–	–	–	–	23.9	21.8	41

Without Amputation.

4	Congenital syphilis.	F	13	15.	16.	6.	5.7	16.	17.8	C.15-D.17-L.18
5	Not insane, .	M	6	14.	18.6	4.9	5.	18.[1]	15.	C.15-D.15-L.16
6	Organic dementia,	M	42	23.	31.8	5.5[1]	6.	37.5	28.	C.16-D.14-L.15
7	Mongolian idiot, .	F	6	11.8	12.	11.6	14.	28.8[1]	27.	C.15-D.26-L.26
8	Idiot, . . .	M	17	43.	52.7	10.7	10.8	29.4	31.	C.18-D.22-L.19
9	Imbecile, . .	F	46	36.	32.	6.	6.	34.	31.	C.18-D.17-L.15
10	Alcoholic, . .	F	38	30.7[1]	28.	6.[1]	6.	33.[1]	37.	C.16-D.17-L.15
11	Auto-intoxication,	F	42	29.[1]	34.	7.[1]	6.	33.7[1]	35.	C.16-D.34-L.18
12	Alcoholic delirium,	F	32	27.6[1]	41.6	6.8[1]	7.	27.	28.6	C.15-D.33-L.18
13	Special control, .	M	37	50.4	54.3	12.	12.9	49.5	52.4	C.67-D.53-L.62
14	Presenile depression.	F	68	23.5[1]	22.5	4.[1]	5.	19.9[1]	17.9	C.15-D.15-L.15
15	Unclassified, .	M	71	19.4	19.6	2.8	3.8	19.	17.8	C.15-D.15-L.15
16	Delirium, . .	F	–	14.9	13.4	2.6	2.5	17.8	19.2	C.15-D.36-L.15
17	Not insane, .	F	51	–	–	8.	8.6	22.7	21.8	D.34-L.14
18	Dementia præcox,	F	40	21.[1]	25.	5.9[1]	5.4	14.[1]	11.	C.21-D.18-L.22
19	Imbecile, . .	M	34	34.3[1]	21.3	11.3[1]	6.3	24.9[1]	23.4	C.20-D.25-L.20
20	General paresis, .	M	39	20.4[1]	20.2	3.[1]	3.1	8.2[1]	8.5	C.20-D.20-L.20
21	Unclassified, .	M	21	–	–	4.	4.	14.[1]	13.5	D.41-L.25
22	Chronic dementia,	F	40	8.9[1]	8.1	1.8[1]	3.	11.[1]	9.1	C.31-D.21-L.33
23	Puerperal mania,	F	24	6.6[1]	7.8	2.1[1]	2.	7.4[1]	8.7	C.21-D.22-L.20
24	Uremic intoxication.	F	28	4.[1]	5.6	1.3[1]	1.9	7.7[1]	6.6	C.23-D.32-L.21
25	Dementia præcox,	F	35	6.5[1]	6.9	1.2[1]	1.2	10.3[1]	10.4	C.20-D.22-L.20
26	Imbecile, . .	M	36	5.5[1]	3.4	2.1[1]	2.2	–	–	C.16-D.17
27	Infant, . .	–	11 mos.	6.9[1]	6.2	3.[1]	3.8	13.[1]	12.6	C.23-D.22-L.22
28	Unclassified, .	F	3 yrs. 10 mos.	–	–	3.[1]	2.7	17.[1]	19.	D.24-L.24

[1] Left side of cord.

These results contribute something also to the question of whether the number of cells is greater on one side or the other from the standpoint of right and left handedness. It will be seen that there is no constant relation throughout the list, the number being greater as an average on one side in some instances, and less on the same side in another, with very slight variation in any case, and no more in the cervical than in the lumbar region. By means of a low-power lens it may be seen in progressing from one section to another that one horn contains the greater number of cells, first on one side and then on the other, and the same variation is seen in the individual cell groups.

It may be noted here that Bruce [19] found only the fifth cord specimen examined suitable for use in preparing his "Atlas of the Spinal Cord."

Summary.

Cell counts were made on the anterior horns of the spinal cord in 28 cases. Three of these were cases following amputation of an extremity. The 25 additional cases were said not to have had signs of a cord lesion.

Variation in the counts between the two sides in the amputated cases was not more than two or three cells in the final average. In two of these the greater number was on the side corresponding to the amputation.

Variation in the counts between the two sides in the cases without amputation was at times greater than with amputation.

In the sections where identification was made of the right and left sides there appears no uniform difference between the two corresponding counts.

Conclusions.

The literature contains a variety of opinions concerning the permanent changes in the anterior horn cells of the spinal cord following amputation.

A fairly large number of counts of anterior horn cells of the spinal cord from cases without amputation show as great a variation in the number of cells as in cases with amputation.

In the material examined there seems to be no constant variation between the number of anterior horn cells in the right and left sides of the spinal cord.

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A CONSIDERATION OF THE NATURE OF AURÆ.*

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Descriptive and statistical studies of auræ are to be found in textbooks of nervous and mental disease, treatises on epilepsy and migraine and special articles, but these sources of information are searched almost in vain for an exposition of the particular conditions of the nervous system or of the mind that favor the occurrence of auræ. Such references as one finds generally are bare statements unsupported by argument, and obviously taken without question from the conclusions of some distinguished investigator. That these references are scarce and unconvincing is not surprising in view of the difficulty of investigating auræ, as well as other phenomena connected with epilepsy and migraine, first hand in the person afflicted.

The subject would seem to be worthy of consideration, however, because without a proper understanding of the underlying conditions it is hardly possible either to form a satisfactory opinion of the relation of auræ to the convulsions in epilepsy, or to the headaches in migraine; or to make an accurate statistical or analytic study of auræ themselves. In this article, therefore, an attempt is made, first, to bring forward objections to what seems to be the prevailing view; second, to point out anew the relation of auræ to a certain mental state, and finally, to suggest some factors that may influence the form the auræ may take.

Auræ of Epilepsy.

Objections to Prevailing View on Auræ. — The notion of auræ that is most popular with the authors of textbooks probably originated with Hughlings Jackson,[1] but is given very clearly and concisely in these words of Gowers: [2] —

> This immediate warning is of the greatest importance. . . . The sensation is the effect on consciousness of the commencing process of discharge, which begins in structures by which these are influenced that are highest

* Contribution in a series offered to Prof. E. E. Southard, in honor of the decennium of the Bullard Professorship of Neuropathology, Harvard Medical School.

in function and related closely to consciousness. The warning is thus an indication of the part of the brain in which discharge begins, because the place where it first attains such an intensity as to cause a sensation must be the place at which it starts. . . . Their interest is great, but their practical value is almost limited to the detection of attacks which might otherwise be unperceived, by the evidence their character affords, and by their frequent indication that the instability is the result of a local lesion of the brain.

There is in this conception of the nature of auræ an application to the sensory component of the epileptic attack of one theory of the origin of convulsions, namely, that which assumes them to be the result of a "discharge" of nervous energy in the motor cells of the precentral area.

Even though this conception of the origin of the convulsive movements of epilepsy be accepted as satisfactory, its application in the explanation of auræ may be objected to. The convulsive movements are of sudden onset, and display little evidence of a co-ordination of nervous processes. On the other hand, the aura may be relatively slow in evolution, and, if complex in nature, indicates a delicate co-ordination of nervous impulses that is inconsistent with the notion of a "discharge." Further, the conception is incomplete in that it does not indicate the relation of the auræ which occur in the presence of an organic lesion to those which occur in brains apparently normal in structure. It is begging the question to get over this difficulty by assuming all cases of epilepsy to be the result of an organic brain disease. Structural changes that probably are not secondary are not found in a large proportion of the brains of a certain type of epileptics. In a still larger proportion the aura is not associated with changes in special sense centers that correspond to the special sense in which the aura occurs. It cannot reasonably be stated, then, that the aura of a special sense indicates or may indicate structural or even functional changes of a pathologic nature in the centers of that sense. A theory of auræ should make clear in how far a particular aura may be determined by structural changes, and where these changes should be looked for.

In view of the relative futility of efforts to investigate auræ first hand in afflicted persons, it is well to attempt to employ another method, *i.e.*, try to get some light from a study of similar and perhaps less inaccessible phenomena, if such can be found, and to apply the information thus obtained by analogy.

There is a mental phenomenon, or rather a series of allied phenomena, of common occurrence in man, namely, hallucinations, to which it would seem auræ could be safely compared. Parish,[3] McDougal[4] and others have noted the similarity of these manifestations of mental activity. Although some conspicuous differences may immediately stand forth, it is apparent that they are not essentially dissimilar. The subject-matter of the one can generally be essentially duplicated in the other. The senses of sight and hearing, moreover, are represented in both in a similar proportion, — as 71 to 29 in some statistics of the occurrence of auræ collected from several sources, and as 70 to 30 in the statistics of the occurrence of hallucinations collected by Parish.[5] The half-recalled memories or "deja vu" phenomena of certain incomplete attacks have many parallels, occurring in connection with sleep and certain waking mental states. No insuperable objection to this comparison is evident, at first sight at least.

Relation of Auræ to Other Hallucinations. — Hallucinations are common in both abnormal and physiologic mental states. Their occurrence in the insane and in those addicted to the use of drugs and alcohol is well known. The most common manifestation in physiologic states occurs in connection with sleep, in the form of dreams. There are also the hallucinations of hypnosis, of crystal gazing and of the psychic medium. Finally, there is the spontaneously occurring variety so much studied by spiritualists, and commonly known as visions.

According to Parish[6] there is a common mental state underlying all hallucinations which he designates "dissociation of consciousness." By this term he refers to a state of consciousness that differs from the waking state, in that normal association of ideas does not occur, or in which, as James expresses it, ideas are "deprived of their reductives." Leaving aside as too complicated for consideration the pathologic state in which hallucinations are found, there is the loss of consciousness to a greater or less degree in sleep, and a similar, but less profound, loss in hypnosis and crystal gazing, which favors the production of hallucinations. That the psychic medium usually gives her information with eyes closed would indicate that she may be at such times in a state of autohypnosis. In the case reported by Prince,[7] visions appeared in a prospective medium only after she had gone through a preliminary course of training, which consisted in gazing intently at a small point on a table for a

long time. She doubtless was thus acquiring the power of auto-hypnosis. In the case of the visions reported by various societies for psychical research, Parish was able to demonstrate that in a large proportion they occurred under conditions that favor sleep, or during emotions such as grief, fear or excitement that may produce a somewhat similar dissociation of consciousness. Before reading the conclusions of Parish I had been impressed with this association merely in going over accounts of visions by various authors.

There is in epilepsy a disturbance of consciousness in the form of a loss. The depth of the unconscious state precludes the recollection of any visions occurring at this time, but there is a brief interval before consciousness is entirely lost that is probably not unlike the normal drowsy state, and during which there are probably conditions which have been shown to be suitable for the development of hallucinations. That hallucinations or auræ do occur at this time is, therefore, not surprising. Hence one should consider auræ as having an origin somewhat similar to that of hallucinations in normal persons, and should not assume, as Gowers and others have assumed, that they result from a "discharge" of an epileptic nature, due perhaps to a local lesion.

Factors influencing the Form of Aurœ. — If this assumption be true, the content of auræ should in general be derived as are dreams and visions. They may represent a fragment of memory, as was the case with one patient of mine whose aura consisted of a familiar face, — not always the same face, however, — and with another, whose aura was the vision of a disagreeable old woman he had known in childhood. In this connection it is interesting to recall the suggestion of Schwab [8] that auræ may represent memory pictures of events attending the first fit, which have been "fixed," so to speak, by the strong attending emotional reaction. Further, the aura may consist of diminution or distortion of normal perceptions — micropsia, macropsia, etc. — which occurs also in connection with sleep. Finally, the underlying factor may be structural change. Since disease of the organs of special sense or of their pathways leading to the brain may lead to the formation of hallucinations in the corresponding sensory spheres in either the sane or the insane,[9] similar changes may influence auræ. Turner [10] considered these factors, in the case of auditory auræ, without much success, but the subject is worthy of further study.

Some points at which auræ and other varieties of hallucinations differ are worthy of consideration. There is, first, variability, auræ being constant in most cases and hallucinations generally fleeting. This difference may be in part explained by one of the characteristics of epilepsy, namely, stereotypy. In general, the various reactions in epilepsy tend to be constant; hence, the preconvulsional disturbance of consciousness should be about the same in all attacks. This being true, the aura would be expected to be relatively constant. On the other hand, drowsy states vary within the widest limits, and in them, unlike epileptic mental states, consciousness is often very receptive to external stimuli. It is therefore not surprising that the hallucinations should vary. Another point of difference is the absence of hallucinations during and after the convulsion. The depth of unconsciousness and fatigue factors may account for this lack. Some authors have assumed, however, that hallucinations do occur at this time.

Auræ of Migraine.

As regards migraine, the problem is more obscure. Parallels for some of the auræ of migraine, such as the fortification spectrum described by Gowers, for instance, are rare; but as auræ of this type seldom appear, few parallels should be expected. In visions and hallucinations bright lights and brilliantly colored objects are not unusual. Not unlike some migrainous auræ is the vision of the boy, described by Gurney,[11] who saw in the dark a distant, tiny, luminous point approaching and increasing in size and becoming a face, and finally a mass of luminous faces unlike anything he had ever seen. A patient of mine had, after retiring and before falling asleep, a vision consisting of a "head of flame." That some disturbance of consciousness occurs with migraine there can be little doubt. Migraine is regarded by many as akin to epilepsy, and various abnormal sleep-states are commonly associated with it. One would think that conditions in migraine are even more favorable for the formation of hallucination than are those in epilepsy, inasmuch as in migraine the march of symptoms is slow, and consciousness is not lost.

There remains to be considered the relation of the localized brain lesion to auræ. That there is an association of olfactory auræ with certain local lesions, Hughlings Jackson,[12] Gowers [13] and Southard [14] have conclusively demonstrated. This fact, instead of controverting the view that auræ are merely a type of hal-

lucination, is itself made clear by some characteristics of hallucinations. It already has been pointed out that lesions of organs of special sense or of their pathways leading to the brain may predispose to aura formation. In the case of the brain lesion, then, it may be assumed that the same principle is at work, the only difference being that interruption of peripheral impulses occurs in the brain rather than in the peripheral pathways. Indeed, this principle can be applied in instances where another, let us say that of direct irritation to the cortical cells, cannot be. In a case with olfactory auræ described by Jackson,[12] for instance, the lesion found post mortem was a cyst of softening in the hippocampal gyrus. According to a dictum of Jackson himself, a purely destructive lesion should not be considered as acting as an irritant on surrounding cortical substance. Again, in a case with a similar type of aura, quoted by Gowers,[13] the lesion found at necropsy was a gumma of one olfactory lobe. In neither of these cases, then, can the aura have resulted from an irritation of the olfactory cortex, but both are easily explained as the result in the center of a disturbance of incoming nervous impulses.

Conclusion.

By way of summary it may be stated that I have attempted to point out anew the analogy between auræ and the hallucinations occurring in connection with sleep, hypnosis, crystal gazing, etc. According to this view, auræ should be regarded not as the result of "discharges" of an epileptic nature in some part of the cortex, but as deficiency reactions, like dreams, occurring when there is a "disturbance of consciousness" of a certain type. Their relation to the loss or disturbance of consciousness in epilepsy and migraine is assumed to be the same as that of dreams to drowsy or sleep states; and their content should be regarded as being determined by the same factors that determine the content of dreams and similar hallucinations. Their relation to structural changes may be the same as that of those hallucinations which develop in connection with disease of the organs of special sense or of the nerves connecting them with the brain.

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BRAIN TUMORS AS SEEN IN HOSPITALS FOR THE INSANE.*

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It is not a rare experience for the pathologist in a hospital for the insane to find at necropsy a brain tumor undiagnosed during life. The objects of this paper are to inquire into the reasons for the lack of diagnosis, and to find out whether the group of brain tumor cases in hospitals for the insane presents any special characteristics as to symptomatology, age or stage of disease on admission, which would distinguish them from cases in general hospitals.

All brain tumor cases coming to necropsy during the past ten years in the Boston, Danvers, Taunton, Westborough and Worcester State hospitals and the Psychopathic Hospital were studied, as were also single cases at the Medfield, Foxborough, Bridgewater and Northampton State hospitals. Gummas were excluded. The histories and necropsy protocols of 46 cases thus collected were studied, and in most instances the brains were examined in frontal sections. In about half of the cases the brains and cords were also studied histologically.

The percentage of brain tumors as compared to the total number of necropsies agrees fairly closely in the different institutions: Boston State Hospital, 1.9; Danvers State Hospital, 1.3; and Westborough State Hospital, 2.6. These percentages are about the same as that found by Cushing [1] in the Johns Hopkins Hospital necropsy records up to January, 109, namely, 1.7 per cent.

The age incidence of patients with brain tumors in the State hospital groups presents an interesting and significant deviation from that of such patients in general. The distribution by decades is: from eleven to twenty years, 1; from twenty-one to thirty, 3; from thirty-one to forty, 4; from forty-one to fifty, 18; from fifty-one to sixty, 13; from sixty-one to seventy, 5; from seventy-one to eighty, 1; from eighty-one to ninety, 1.

The average age is fifty years. Bruns [2] states that brain tumors are most frequent from puberty to thirty years, then

* From the Laboratory of the Boston State Hospital. Contribution in a series offered to Prof. E. E. Southard in honor of the decennium of the Bullard Professorship of Neuropathology, Harvard Medical School.

from thirty to forty years; more than half of his cases occurred between the twentieth and fortieth years. He, however, includes tubercles and gummas, so that the two series are not strictly comparable. In Cushing's series of 130 cases the maximum number occurred between the twentieth and fortieth years. It appears, however, that the average age of patients with brain tumor sent to hospitals for the insane is greater than that of brain tumor patients in general.

The sites of the tumors, in order of frequency, were: frontal, 15; temporal, 6; multiple (metastatic), pituitary and intraventricular, 4 each; cerebellar or cerebellopontile, 5; central fields, parietal and corpus callosum, 2 each; occipital and peduncular, 1 each. The large proportion of frontal tumors (33 per cent) is significant, as in the statistics of Schuster [3] for brain tumors in general, cerebellar growths lead, with a percentage of 21.6; followed by multiple, 14.7 per cent; frontal, 12.1 per cent, and central, 12 per cent.

TABLE 1. — *Sources of Group of Patients with Brain Tumor sent to Hospitals for the Insane.*

Sent by private physicians (undiagnosed),	31
Sent from general hospitals (undiagnosed),	6
Sent from general and special hospitals (diagnosed),	2
Sent from general hospitals after operation for brain tumor,	2
Developed in patients in hospitals for the insane,	4
Voluntary admission,	1
	46

TABLE 2. — *Stage of Disease at which Patients were admitted.*

Early, that is, soon after the appearance of the symptoms, [1]	4
Advanced, the symptoms dating back from one and a half to three years, and the patients living from one to four years after commitment,	8
Greatly advanced, the patients surviving only a few months after admission,	19
Terminal,	11

TABLE 3. — *Symptoms necessitating Commitment.*

Simple deterioration (neurologic signs also present),	10
Convulsions, with or without mental deterioration,	4
Confusion, hallucinations and disturbances of memory, the latter appearing as transitory amnesia, a general reduction of immediate and remote memory, or an almost total loss of immediate retention,	9

[1] One patient was sent to an institution for epileptics and later to a hospital for the insane.

Lethargy and somnolence, ... 8
Symptoms of psychosis (manic-depressive, dementia præcox and senile dementia) antedating symptoms of tumor, but the latter present at time of admission, ... 5
Aphasic and apraxic disturbances, ... 3
Predominantly physical disabilities (blindness and deafness), with irritability and mild paranoid trend, ... 2
Confusion and physical weakness, ... 1

The diagnoses made after the patients reached the hospitals for the insane revealed the small percentage of cases in which the correct diagnosis was made and the conditions with which brain tumor was confused. The diagnoses were: brain tumor, 15; "organic dementia," 8; cerebral arteriosclerosis, 4; epilepsy and paresis, 3 each; cerebellar disease, 2; cerebral hemorrhage, Korsakoff's psychosis, manic-depressive and dementia præcox, 1 each; unclassified, 2; senile dementia, 2.

Mistakes in Diagnosis.

The diagnosis of brain tumor was made in only one-third of the cases (including four admitted from other hospitals with the correct diagnosis). The cases diagnosed as paresis would probably be correctly diagnosed at the present time, with the routine examinations of the spinal fluid now general in hospitals for the insane. Tumors in senile persons are difficult to diagnose. Mistakes in diagnosis tend to fall into three groups: deteriorated cases with neurologic signs are called paresis, Korsakoff's psychosis, or put into the catchall of "organic dementia;" cases presenting focal signs are confused with arteriosclerosis; and those with convulsions are merely called epilepsy.

A surprisingly small proportion of cases of brain tumor are diagnosed correctly. There are several reasons: First, the training and point of view of the physician in a hospital for the insane is psychiatric rather than neurologic, and he is preoccupied with the mental symptoms. In general hospitals, of course, the reverse tendency prevails. Second, the most fundamental reason is that, as a rule, ophthalmoscopic examinations of patients presenting organic signs are not made unless brain tumor is definitely suspected. If such examinations were made, a much larger percentage of tumors would be diagnosed, and until they are made as a routine measure, the percentage of cases of brain tumor diagnosed will not be much raised. It would appear that

there is no more reason for neglecting this diagnostic aid in any organic case than for omitting a Wassermann test. Third, the use of the term "organic dementia" as a sufficient designation discourages any refinement of diagnosis. Fourth, the group of tumor cases seen at State hospitals offers peculiar liability to confusion in diagnosis. A large proportion of the cases occur in middle age when deteriorating psychoses, such as paresis, Korsakoff's psychosis, and cerebral arteriosclerosis, are common, and are naturally first considered. This is particularly true of cerebral arteriosclerosis, which frequently coexists with brain tumor; when it occurs, the exclusive diagnosis of arteriosclerosis is apt to be made to cover all symptoms.

A study of the frequency of arteriosclerosis was made in all the available brains of this series. In 18 of 39 there was notable arteriosclerosis, both of the basal and of the small cortical vessels, all in persons of the fifth decade or beyond. In 8 the degree of arteriosclerosis was advanced, and in 3, small cysts of softening were present.

A microscopic study of the brain was made in 19 cases. The changes in regions not immediately affected by the tumor were not uniform, nor were they striking, aside from the cases in which arteriosclerosis was present. Lamination was well preserved, but the cells were sometimes askew in arrangement. Chromatolysis was occasionally present, as was an increase of satellites and perivascular pigment. Gliosis, particularly subpial, was frequent in both the arteriosclerotic and non-arteriosclerotic cases.

Certain tumor groups are of particular psychiatric interest, namely, the frontal, temporal, parietal, ventricular and callosal. These will be considered in detail elsewhere, and only a few points touched on here.

Frontal Tumors.

It is difficult to get a clear-cut clinical picture of this group. All of the patients except two (an alcoholic dement and a senile patient) were admitted in the late or terminal stage, and the most prominent feature at the time of entrance was deterioration, usually accompanied by apathy, sometimes, however, by confusion and excitement, and frequently by somnolence. Deterioration was the most pronounced and constant characteristic. The special importance of frontal tumors for the production of dementia is generally assumed, but has been ques-

tioned by Von Monakow,[4] Müller[5] and Bruns, among others, their view being that frontal growths usually attain a large size before encroaching on vital centers, and that the psychic changes attributed to the specific involvement of the frontal areas are in reality due to diffuse injury of the cortex, increase in intracranial pressure, and interference with circulation. This series is not adapted to throwing light on the question because of the advanced stage at which the patients came under observation, and because of the lack, in most cases, of a full history of the early part of the illness. Nor was it possible always to differentiate between "Benommenheit" and true dementia, although the descriptions in most instances leave no doubt that there was real mental reduction.

Müller,[5] in his analysis of 164 cases of frontal tumor, finds that a larger proportion occur in middle life (from forty to sixty years) than is the case with tumors of other regions. The maximum of his curve is at from thirty-one to forty years, 26 per cent, followed by 20 per cent at from forty-one to fifty years, and 16 per cent at from fifty-one to sixty years. The distribution of the State hospital series is: from eleven to twenty years, 1; from twenty-one to thirty, 0; from thirty-one to forty, 2; from forty-one to fifty, 6; from fifty-one to sixty, 3; from sixty-one to seventy, 2; from seventy-one to eighty, 0; from eighty-one to ninety, 1.

The average age is fifty and one-half years. There are no significant differences between the average ages of patients with frontal tumors and those with tumors of other areas (posterior fossa, forty-five and one-half years; all regions except frontal, forty-eight years), but it is interesting to note that the average age for all classes of tumors is above that given by Müller.

Epileptic convulsions were present over a considerable period in 3 patients, frontal ataxia in 3 (causing the diagnosis of cerebellar disease), and in 2 patients there was early the somnolence supposed to be particularly characteristic of frontal growths.

The large percentage of frontal tumors in the State hospital series may be due, not to any peculiar relation between frontal growths and dementia, but to the fact that disturbances from these tumors are, in many cases, not obvious, unless the patients are under close observation (as they usually are not) until a late stage, when the final deterioration necessitates commitment; also, in the absence of striking neurologic signs, the psychic symptoms stand in the foreground, and the patient is sent

to a hospital for the insane rather than to a general hospital. Another factor, that of an increasing tendency to deterioration with advancing age, will be discussed later.

Tumors of Temporal Lobes.

Tumors of the temporal lobes are of special interest on account of uncertainty of the diagnostic features of tumors in these regions. Cushing states that, with the exception of the uncinate area, the temporal lobe is a relatively silent region, even on the left. Several authors have tried to differentiate a syndrome common to tumors of both sides. Foster Kennedy[6] emphasizes the epileptic convulsions and their equivalents of dreamy states; crude, subjective sensations of smell and taste, with or without involuntary movements of mastication; and after the attacks, transient weakness of the contralateral lower facial muscles, less often of the arm and leg, and increase of the deep reflexes. The motor symptoms and reflex changes later become persistent. Albert Knapp[7] gives as a syndrome characteristic of both lobes, homolateral ptosis and mydriasis, contralateral hemiplegia and cerebellar ataxia. Bruns and Aswazoturow[8] consider that periods of auditory hallucinosis may be the equivalent of the convulsions. Mingazzini[9] divides the temporal lobe into four zones, the tumors of each having a characteristic symptomatology. Zone 1 consists of the anterior portion of the convex surface, and its syndrome is total hemiparesis, associated with contralateral ptosis and paresis of one or both abducens. Zone 2 comprises the posterior half of the convex surface. In tumors of this region hemiparesis is almost constant, and all branches of the oculomotor may be affected; also, there is a tendency to conjugate deviation of head and eyes and ataxia of the cerebellar type. If the tumor is on the left, sensory aphasia or dysarthria are present with tumors of both zones. In the third zone, the posterior part of the inferior surface, the most frequent signs are unilateral paralysis of the abducens, isolated paralysis of the facial, contralateral ptosis, hemiparesis and hemianesthesia. Aphasic disturbances are frequently absent. The fourth zone includes the anterior part of the inferior-internal surface, and in tumors of this area hallucinations of taste and smell are common.

Arranging the present cases according to Mingazzini's classification, there were two tumors involving zone 1, the first extending beyond the limits of the zone. The case presents so

many features of interest, both psychiatric and neurologic, that it is given in abstract. The patient, a left-handed person with a left-sided tumor, had also the nearest approach to Witzelsucht of any of the State hospital cases.

Case 1. *History.* — A woman, aged 35, sent to the Boston State Hospital from a general hospital to which she had been admitted with the diagnosis of hysterical hemichorea, had always been flighty and peculiar. For several years previous to admission she had made no effort to work, but lived on her savings. She complained of numbness in the right hand for two or three years; weakness and tremor of the right arm and leg came on suddenly three months before admission. She had had several slight fainting attacks. On admission she was talkative, hilarious and facetious; her replies were relevant but flippant. She complained of her illness, but was not concerned over it, and showed no insight. She was well oriented for person, place and time; her understanding of surroundings was fair. Remote memory was apparently somewhat impaired; her memory for recent events was good. She would not attempt the educational tests. She had no hallucinations or delusions. She was neat and docile.

Physical Examination. — The face was expressionless. Movements of eyes and tongue were normal. The right pupil was larger than the left; both reacted well. Vision was undisturbed. There was no choked disk. Hearing was normal, and power of speech was intact. The right arm and leg were spastic and atrophic with marked coarse tremor, increased on intention. Knee jerks were increased. Sensation to touch and pain was normal.

Course of Disease. — The patient remained at the hospital for two and a half months. She had alternate periods of drowsiness and exhilaration; during the latter she laughed and talked much of her suffering. She had severe occipital headache. The temperature was continuously subnormal; pulse rate, 80–100; respiration, 20–25. Death occurred suddenly in syncope. No definite diagnosis was made, either at the general hospital or at the hospital for the insane.

Necropsy. — Necropsy revealed a very large cholesteatoma, which had destroyed the anterior half of T1 and T2, the transverse temporals, the lower border of Broca's area, the lower part of the insula, the pyriform lobule, the anterior half of the hippocampus and the subthalamic structures on the left.

Case 2. *History.* — The second case was an endothelioma involving the anterior part of the right temporal lobe in a woman aged 57. The illness began two years before death with a change of character, the patient becoming moody, suspicious and irritable and showing defective judgment. Weakness of both legs developed into spastic paralysis; she had general convulsions every three or four weeks. In the hospital she had periods of confusion, alternating with comparative clearness, euphoria and facetious-

ness; also episodes of auditory hallucinosis, to which she responded energetically. Dysarthria, double ptosis and conjugate deviation of the eyes to the side of the tumor were noted. This case was complicated anatomically with cerebral arteriosclerosis.

The tumor involving zone 2 has been reported by Fuller.[10] The growth was on the left, sensory aphasia was prominent, and auditory hallucinosis was mentioned. The neurologic signs were divergent squint, exophthalmos and bilateral choked disk.

The third zone was involved in two instances. The symptoms in the first patient, a man of fifty-seven, were nervousness, irritability, insomnia, possibly auditory hallucinosis, right-sided headache, unsteadiness of gait and tremor. The neurologic symptoms were marked exaggeration of all deep reflexes, general increase in muscular tonus, general tremor, right-sided facial spasm and left Babinski reflex. The tumor involved both the third and fourth zones on the right, extending from the tip to the splenium, destroying also the hippocampus, and extending upward, invading the insula and all structures up to the lenticular nucleus.

The second case is taken up in the discussion of tumor in senile patients.

The fourth zone was the site of a tumor in one instance. The patient was an imbecile of fifty-eight, who had deteriorated rapidly in the two years before death. She had olfactory hallucinations, at times calling out continuously, "Oh, that bad smell!" Seven weeks before death she had a convulsion followed by weakness of the right side and involvement of speech. The tumor, a metastasis from a hypernephroma, involved the inferior and mesial surfaces of the left temporal pole.

Each of the cases quoted above presents features of the syndromes of Kennedy, Knapp and Mingazzini, but no one case corresponds closely to any of them.

The only instances of pronounced euphoria in the entire State hospital series are the two temporal tumors mentioned above.

Tumors of the Corpus Callosum.

The two patients with tumors of the corpus callosum, involving the entire length of the structure, but not limited to it, showed marked mental changes. In the first patient there was increasing slowness of reaction, with somnolence, but his answers were coherent and relevant, and showed comprehension; recent

and remote memory was good, and school knowledge was retained. Paralysis of the legs occurred late in this disease. The tumor infiltrated laterally into the right frontal lobe. In the second patient the first and the predominating symptom was loss of memory, which progressed until a few months before death there was absolutely no immediate retention. The patient was confused and completely disoriented. Two months before death optic aphasia was noted. The tumor swept out laterally into both parieto-occipital regions. In neither of these cases was there involvement of the cranial nerves.

Tumor of the Ventricles.

There were four cases in which the tumor (a glioma in each case) was wholly or almost wholly within the lateral or third ventricles. These cases were characterized by profound mental symptoms, in three cases, prominence of the general symptoms of tumor and abundance of neurologic signs. In two cases there was a gradual failure in all mental functions, without active manifestations, and reaching an extreme degree. The third case was complicated by an independent manic-depressive psychosis. The fourth was characterized by increasing lethargy with transient periods of amnesia and confusion, but without true dementia. There was some similarity in the physical signs, the most prominent being unequal pupils, with sluggish reaction to light, in three cases; exaggerated reflexes in three, spasticity in two, tremor in all, and marked ataxia in three cases. Weisenburg,[11] in his article on tumors of the third ventricle, emphasizes the prominence of symptoms of internal hydrocephalus, the marked mental symptoms, the paresis and spasticity, and the ataxia which is present in nearly all cases.

Mental Symptoms.

It is fair to assume that because they were sent to hospitals for the insane the patients studied represent a selected group in which mental symptoms were, to the committing physicians, the most prominent feature of the disease.

The predominance of mental symptoms was due, in a part of the group, to a coincident psychosis of one of the common forms. Thirteen of the patients had been recognized as mentally abnormal — either defective or psychotic — before the development of the tumor symptoms. Three were already in hospitals for the insane, and one was committed after operation

for brain tumor. In the other instances the primary psychosis caused the patients to be committed. There were, however, well-developed organic signs in all of the latter cases at the time of entrance. The psychoses represented were: manic depressive, dementia præcox, paranoid condition, senile dementia and alcoholic dementia. In three cases, at least, it seemed to be the development of the tumor that precipitated the active symptoms of the psychosis, and thus necessitated the final commitment.

Excluding the cases in which there was an independent psychosis, with its own characteristic symptoms, and those patients admitted with terminal lethargy and somnolence, in a review of the mental symptoms one is impressed by their undetermined character, the symptoms being most frequently a simple deterioration in all mental functions with apathy, varied occasionally by periods of confusion or slight euphoria. These symptoms occurred with tumors in various situations. Hallucinosis was sometimes mentioned, but was not a prominent feature, except in the temporal lobe tumors. Disturbances of memory were emphasized in the majority of cases; most frequently there was a diminution or even total loss of immediate retention, in other cases, transitory periods of amnesia. The memory disturbances were most extreme in a tumor of the corpus callosum, and in one filling the ventricles and associated with an extreme increase of intracranial pressure. In the temporal tumors, as mentioned above, emotional changes were prominent. No pronounced depressions, and no neurasthenic, hysterical or developed paranoid states, were found.

It appears that this deteriorating tendency which is so prominent in the State hospital group depends not only on the site of the tumor, but is to some extent characteristic of brain tumors in middle life. Of the 20 cases in this group between the ages of forty-five and sixty, with no independent defect or psychosis, 12, or 60 per cent, presented a picture of apathetic deterioration, while of the 9 similar cases below forty-five years, only 3, or $33\frac{1}{3}$ per cent, presented a similar picture (two of them frontal tumors). A psychiatric study of a group of young patients with brain tumor in a general hospital would be valuable to contrast with these mature patients. Of the 4 patients under thirty in the State hospital series, 2 were imbeciles and the other 2 were admitted in the terminal stages of the disease. It is precisely these deteriorating, middle-aged patients who

would gravitate naturally to hospitals for the insane. This explains why the average age of the State hospital patients is greater than that of brain-tumor patients in general.

Schuster goes to considerable lengths in correlating particular mental symptoms with tumors of different regions. We cannot come to any such definite conclusions as he does regarding the association of complex mental reactions with the involvement of certain locations. In fact, the very lack of clear-cut psychiatric pictures is the prominent feature in this series.

Brain Tumor in the Aged.

There were three tumors in persons seventy years of age or over, the oldest being eighty-six. Only one patient, a man, aged seventy, an alcoholic for many years, had symptoms referable to the tumor. On admission he was confused, irritable and suspicious. His answers were incoherent and irrelevant. Recent and remote memory was markedly defective, and school knowledge was entirely lost. There was disorientation for time and place. The physical findings were advanced peripheral arteriosclerosis, emphysema, general hyperesthesia, particularly along nerve trunks, exceedingly active knee jerks and fine tremor of the fingers. The patient had convulsions at intervals of a few weeks during his two years' stay in the hospital. The first of these began in the right arm and leg, but later they became generalized. He complained first of headache and nausea following the seizures. A year before death aphasia of the motor type appeared with increasing dementia and feebleness. The tumor was a large glioma of the left prefrontal region.

The second case was that of a woman of seventy-two, probably an old dementia præcox, and a hospital inmate for many years. She had had for a long time alternate periods of apathy and extreme excitement, and after one of the latter failed gradually, without special signs or symptoms. The tumor, a glioma, was situated on the under surface of the right temporal lobe, invading also the hippocampus and the pyriform lobule. The brain also showed marked arteriosclerosis with small softenings in the thalamus and the lenticular nuclei.

The third case ran its course as an ordinary senile dementia, complicated with chronic nephritis and arteriosclerosis. Mental failure was said to have begun at seventy-five years. During his nine months' hospital residence the patient was bedridden, quiet, contented and completely disoriented for time and place.

Recent and remote memory was poor, and there was some fabrication. No significant neurologic signs appeared. Failure was gradual. The tumor was a large endothelioma on the orbital surface of the left frontal lobe, protruding into the ventricle. The brain showed the microscopic changes of senile dementia, including plaques.

The reason for the lack of symptoms in some senile brain tumor cases may be that the normal senile brain atrophy lessens the tendency to increased intracranial pressure, and that tumors at this time of life might be expected to grow slowly. In regard to the first point, these senile brains showed flattening of the convolutions only in the vicinity of the tumor, and atrophy elsewhere.

It is obvious that brain tumor patients at State hospitals do not in general offer good prospects for operation, on account of the inaccessibility of the majority of the growths, the late stage of the disease, and the frequent complicating factors, especially arteriosclerosis. Nevertheless, decompressive operations would in many cases have added to the patients' comfort. All patients in State hospitals diagnosed as having or suspected to have brain tumor should be examined by a neurologic surgeon, and the possibility of operation considered.

Conclusions.

Brain tumors occur in general hospitals and in hospitals for the insane with about the same frequency.

The group sent to hospitals for the insane is composed partly (30 per cent) of patients recognized as defective or psychotic before the development of the tumor, and partly of those in whom mental symptoms appear with the tumor.

The average age of patients with brain tumor sent to hospitals for the insane — fifty years — is greater than the age at which brain tumors usually occur; 68 per cent of the cases in these hospitals occur in patients between forty and sixty years.

Frontal tumors predominate, forming 33 per cent of the cases.

The majority of patients are admitted in the late stages of the disease, and the condition is diagnosed, even tentatively, in only about 25 per cent of the cases (excluding those admitted to the hospitals with the diagnosis).

The chief reasons for the small proportion of cases diagnosed are that more emphasis is laid on the psychiatric than on the neurologic aspects of the case; that ophthalmoscopic examinations are not made as a routine measure in organic cases; and

that, as the majority of the patients are middle-aged or elderly, there are frequently complicating factors, both mental and physical, which would be absent in younger persons.

Cerebral arteriosclerosis is a complication, at least anatomically, in somewhat less than half the cases.

In brain tumor of middle-aged patients committed to hospitals for the insane the usual predominating mental symptoms are simple deterioration and apathy. These were most prominent in the frontal tumors, but were present also in those of other areas, with the exception of the temporal tumors, in which the symptoms were more active and varied. This tendency to deterioration appears to be especially characteristic of brain tumors in middle age.

The development of a brain tumor may be the factor which determines the onset of an independent psychosis in a predisposed person.

In old age, brain tumors may reach a large size without giving characteristic signs or symptoms. The reasons for the atypical course appear to be the senile brain atrophy counterbalancing the tendency to increased intracranial pressure, and the probable slow growth of the tumor at this age.

It is earnestly urged that the possibility of brain tumor be more frequently considered in insane patients; that ophthalmoscopic examinations be made in all atypical organic cases; and that when brain tumor is diagnosed, the question of at least a decompressive operation be considered.

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THE USE OF THE THERMOMETER IN MENTAL DISEASES.

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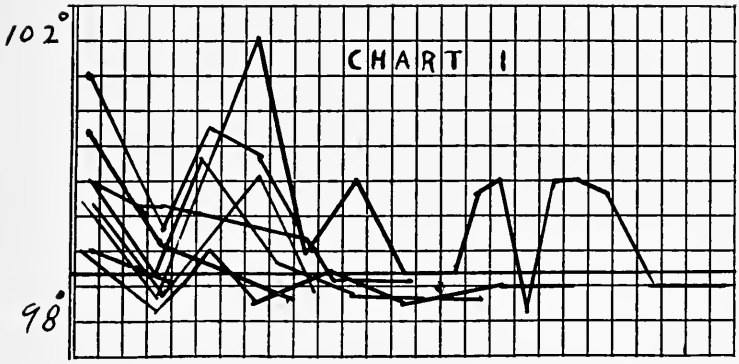
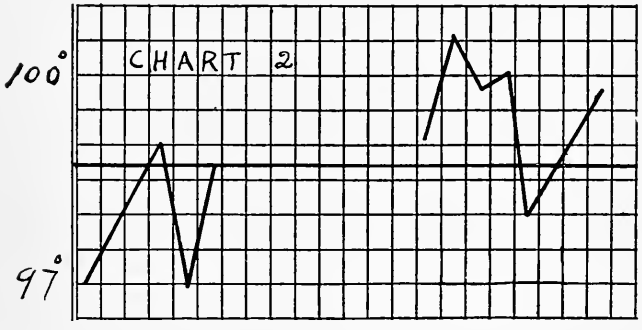
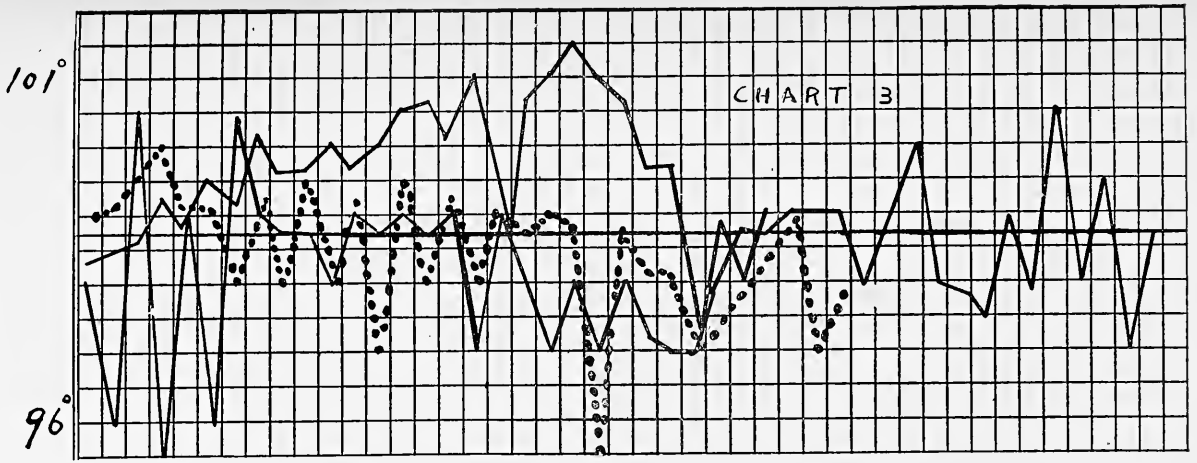
Not long ago the thermometer was considered of no value in mental diseases. There was a tradition that the insane never got fevers. At present there is recognition of the importance of temperature records among the insane, but not enough. The general practitioner, if he meets the mental symptoms of the case first, seems to forget all about his thermometer and stethoscope. Even on the chronic wards of the hospitals for the insane, I suspect that more fevers would be shown if records were made more as a routine, and also if it did not take so much time and trouble to get records upon disturbed and resistive patients. On an admission ward, however, fevers occur frequently, and here and in the practice of the psychiatrist are to be found the opportunities for the further study of the relation of increased bodily heat to mental diseases.

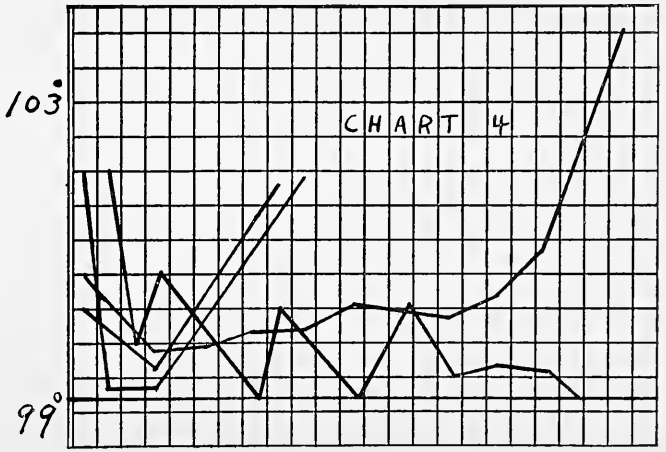
From Jan. 1, 1916, to the first week in July, 71 women were admitted to the Department for Mental and Nervous Diseases of the Pennsylvania Hospital. Fevers slight or severe, transitory or chronic, occurred in over 50 per cent, a surprising result for consecutive cases. Undoubtedly selection has had some part in determining this percentage, physicians perhaps tending to send deliria of certain grades to us, and the hospital making certain discriminations in favor of acute cases. The diagnoses, however, are sufficiently varied and show that fever has occurred in imbecility, epilepsy, arteriosclerotic dementia, general paralysis, dementia præcox and manic-depressive psychoses. Of 19 cases of manic-depressive insanity, 13 had fever and 6 did not. Of 19 cases of dementia præcox 8 had fever and 11 did not, this being the only disease in which normal temperatures were found more often than the reverse.

This paper is an examination of the temperature charts found in these consecutive cases, singly and in groups. We have first a group of several initial fevers of from two to three degrees, subsiding to normal in from one to eight days. This group is shown in composite on chart 1. We can see that such initial


102°
CHART 1
98°


100°
CHART 2
97°


101°
96°
CHART 3


103°
99°
CHART 4

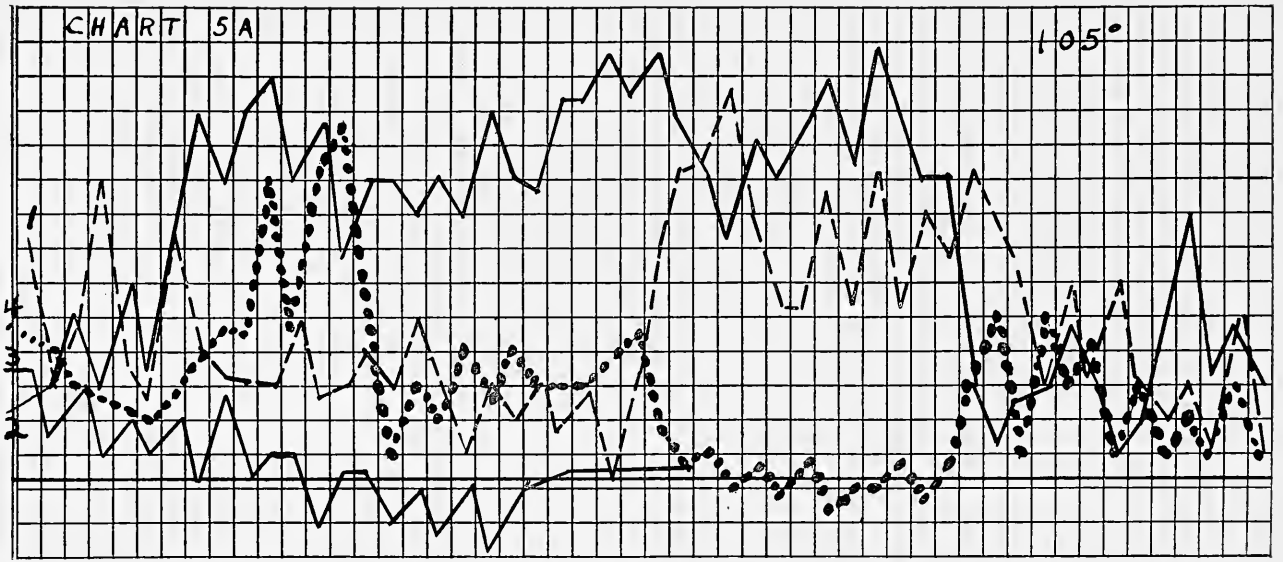
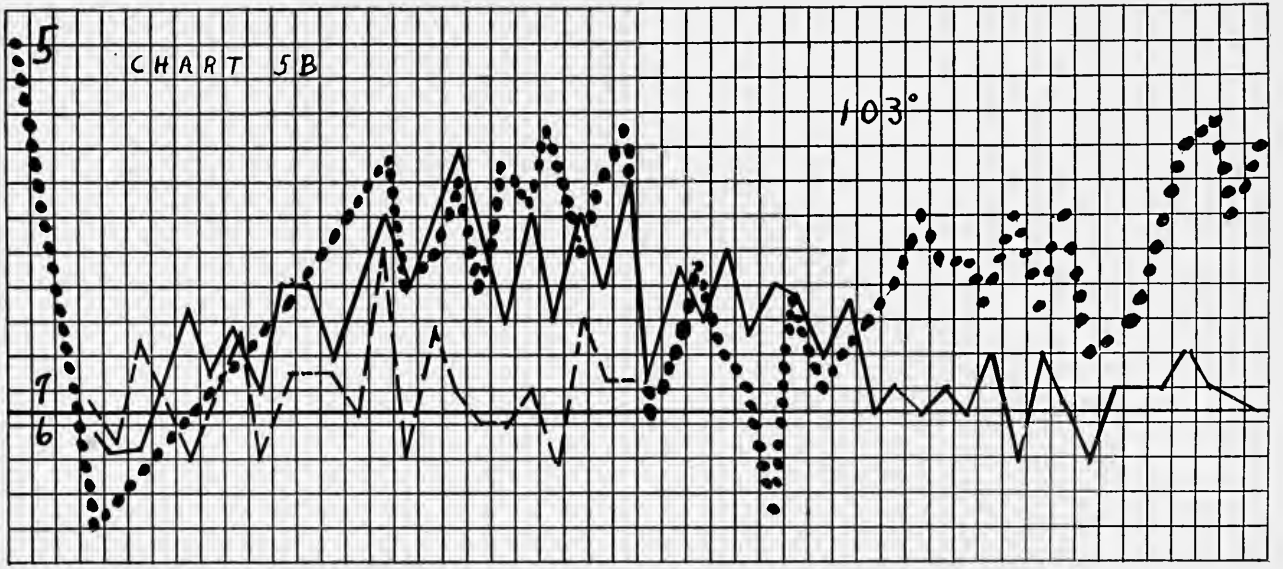
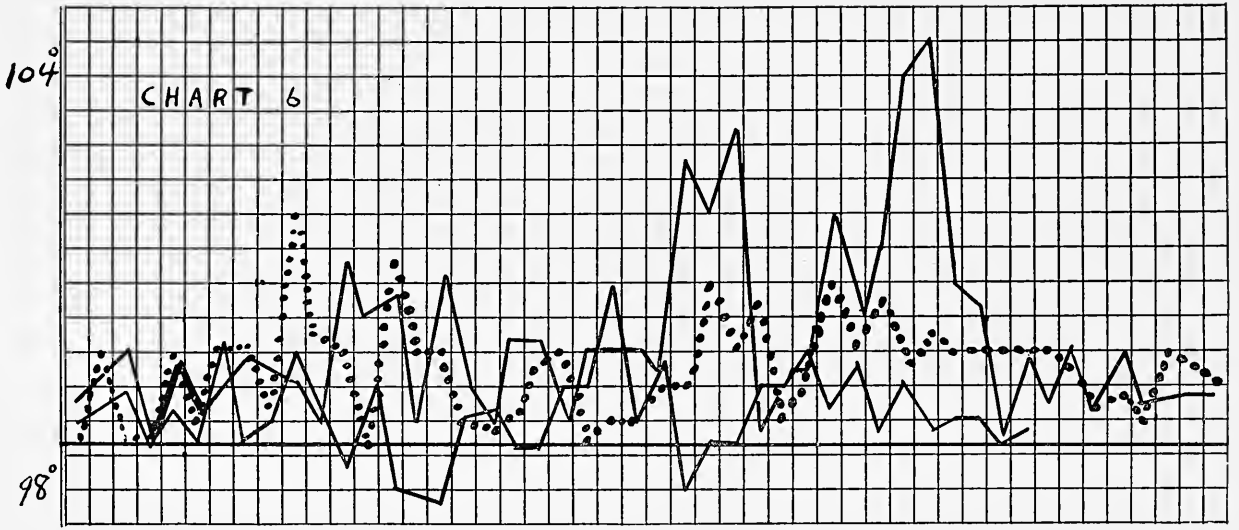


CHART 5A
105°


5
CHART 5B
103°
7
6


104°
CHART 6
98°

temperatures have little meaning for the mental disease. A drop to normal coincides with the coming of the patient under control, after the family, with insufficient advice and help, has allowed the patient to become constipated, or superficially infected from dirty teeth, nails or skin. Noticing the fever, however, is of value in emphasizing the need of immediate treatment; while such conditions undoubtedly mean little if treated, they may mean much if neglected.

It has been our custom, after getting the temperature to the normal line for a few days, to discontinue the chart to the time when clinical indications arise for renewing it. In certain cases, however, we have picked up fevers by taking records without such clinical indications. Such a record as chart 2 shows what happens sometimes, and suggests that the routine use of the thermometer should continue at least through the first menstrual period. The use of the full monthly page of the average temperature chart, even with continued normal findings, seems justified as a routine measure.

A group of three long-continued temperatures in general paralysis cases is shown in chart 3.

Illustrations of fever in all sorts and conditions of defect and disease are supplied freely in the remaining cases; in an imbecile, for instance, at the menstrual period, and in five cases of gross cerebral damage (chart 4).

I turn now to a group of seven cases, the first of which is undoubtedly to be classified as an infective psychosis, and the last as a true manic state. It is the sequence of these cases that I wish to emphasize, with special reference to the physical factors at the onset and the gradual changes in intensity and number of certain, often recurring, symptoms.

A short account of each of these cases is needed and will be found below, while the fever line is given in chart 5 A and B with the appropriate number. The following characteristics for the whole group may be mentioned: This was the first attack for all cases, except the last; the ages at onset ranged from twenty-six to forty-nine; the Wassermann reaction was negative for all seven cases, although the fourth case had had syphilis three years ago, followed by thorough treatment; none of the cases used alcohol.

NONCONCOMITANCE OF SPINAL FLUID TESTS.*

By H. C. Solomon, M.D., Boston.

Tests applied to Spinal Fluid in Diagnosis of Disease of Central Nervous System.

There are five laboratory tests commonly applied to the spinal fluid in the diagnosis of disease of the central nervous system, namely: (1) Wassermann reaction; (2) test for globulin; (3) test for increased albumin; (4) cell count (increase called pleocytosis); (5) Lange's colloidal gold test. A positive Wassermann reaction in the spinal fluid is practically specific for neurosyphilis. A positive result in the other tests, in a general way, proves a pathologic reaction of an inflammatory nature in the central nervous system. At any rate, where an inflammatory condition of the nervous system exists tests 2, 3, 4 and 5 are usually positive. In other words, in meningitis, encephalitis, tumor with meningitis sympathica, vascular insults with secondary inflammatory reaction, traumatic injury and multiple sclerosis these four tests are generally positive. In paretic or tabetic neurosyphilis all five are usually positive.

The subject of this paper is the consideration of the relation of these tests one to the other, the identity or non-identity of one to the other, and their independent appearance and disappearance in disease conditions. There are three methods of study applicable to this problem: (*a*) chemical and biologic analysis of the substances; (*b*) review of the spinal fluids obtained from a large series of cases with attention to anomalous or unusual relations or non-relations of findings; (*c*) frequent examination of fluids from cases of neurosyphilis undergoing treatment, and in which the spinal fluid findings are influenced in the process of improvement.

Wassermann Test.

The Wassermann reaction in the spinal fluid is a biologic reaction pathognomonic of syphilis of the nervous system. As a rule, when present it indicates an inflammatory change in the nervous system, but occasionally it is positive, when the involvement is chiefly vascular and not inflammatory. The so-called

* From the Massachusetts State Psychiatric Institute, Boston. A paper presented to Dr. E. E. Southard, in honor of the decennial of the Bullard Professorship of Neuropathology at the Harvard Medical School.

Wassermann bodies, whatever that substance is which produces deviation of complement, is an unknown element. There is some evidence to show that it is related to the albuminous content of the blood serum, and by analogy, therefore, to the albuminous content of the spinal fluid. Thus Bruck has shown that an albumin reaction occurs in many cases, giving a positive Wassermann reaction which is different from that obtained in Wassermann negative cases. Weston showed that the Wassermann-producing substance does not pass through a dialyzing thimble which is impermeable to albumin. In some unpublished work at our laboratory we have shown that the addition of pure globulin to a spinal fluid giving a negative Wassermann reaction will cause the reaction to become positive. However, these bits of evidence are far from conclusive that the Wassermann-producing body is contained in the albumin, and there is evidence, such as that brought forth by McDonagh, that it is a lipoid element with which the Wassermann reaction is associated. The evidence we bring in the body of this paper is against the relation of the Wassermann reaction to globulin or albumin.

It is, of course, evident that there is no relation between the Wassermann reaction and pleocytosis. Pleocytosis is evidence of inflammation, the Wassermann reaction of syphilis. Even where the inflammation is of syphilitic origin, the Wassermann reaction may be negative in the presence of a pleocytosis, or, what is much more common, the pleocytosis may be absent with a positive Wassermann.

Test for Globulin.

Globulin by definition is an albumin which is salted out of solution by half saturation with ammonium sulphate. Globulin does not occur normally in the spinal fluid. When present it is an evidence of pathology, and it is usually considered as proof of an inflammatory type of reaction. It also may be present, however, when there has been seepage of blood into the spinal fluid through a hemorrhage or vessel changes. If globulin is present in the spinal fluid, theoretically it means that there is an increase in the total amount of albumin, as this is an addition of an albuminous substance to the albumin normally present. As albumin which is precipitated by an acid such as trichloracetic is normally present in the spinal fluid in small amounts, it is increased in amount whenever globulin is present. However, it is not dependent for its increase solely on globulin, but is increased as a result of inflammation. While we have mentioned that increased globulin cannot exist without a theoretic increase

in the amount of albumin, albumin can be present in increased amount without the presence of globulin. We will later show that this actually occurs. While, again, the globulin, albumin and pleocytosis are evidence of inflammation, it does not follow *à priori* that they are dependent one on the other or must be present together. They are quite different elements. The same is true of the Wassermann in relation to globulin and albumin.

Colloidal Gold Test.

The chemical nature of the substance which produces the colloidal gold reaction is not clearly defined. The colloidal gold reaction is a method of differentiating albumins, and was used by Lange in the endeavor to classify the type of globulin occurring in the spinal fluid. Without having succeeded in making this classification, he did discover this practical test. An obvious assumption is that the test is dependent on the albumins or globulins in the spinal fluid. It is probable that the actual type of reaction obtained is dependent to some extent on the balance of globulin and albumin present in the fluid. However, it seems to be a fact that it is not the globulin ordinarily present that causes the precipitation of the gold. Matskiewitsch attempted to identify the substance causing the colloidal gold reaction as peptone. Weston disagrees with this finding. Our clinical experience has shown that the gold reaction may be obtained with a fluid that gives no precipitation with half saturated ammonium sulphate.

Our assumption in this consideration is that these substances may appear independently one of the other, and that while, on the whole, they represent reaction substances of inflammation, they are in some respects entirely different responses.

Spinal Fluid Findings.

Now if this be so, that these substances may occur independently one of the other (with the one exception that globulin means an increase of albumin), it would follow that a number of combinations can occur, and as a matter of fact do occur. Our evidence is derived from two sources, — the routine examination of several thousand fluids, and examination of spinal fluids from cases of neurosyphilis undergoing treatment.

From the first group are obtained instances of the independent appearance of the several elements, and their appearance in various combinations. From the cases under treatment one finds that one test or another disappears first, and finally only

one may be left positive. The different combinations appearing in these two groups are shown in the accompanying table.

Brief examples may be given of the reactions occurring in group 1. The Wassermann reaction occurs independently of other tests, not infrequently in the endarteritic forms of cerebral syphilis. It occasionally is found as the only positive test in cases of congenital syphilis, tabes and diffuse neurosyphilis. On the other hand, we have seen cases in which it was the only test to be absent. This, of course, is always true in non-syphilitic inflammatory conditions giving a positive reaction for the other tests. We have also seen it even in cases of general paresis, tabes and congenital syphilis.

Results of Spinal Fluid Tests.

Spinal Fluid Finding.	Condition in which this Finding occurred (Untreated Cases).	Findings occurring in Treated Cases of Neurosyphilis.
Pleocytosis. Albumin.	Congenital syphilis, undiagnosed mental disease. Trauma, Korsakoff's psychosis, undiagnosed mental disease.	
Wassermann reaction.	Vascular neurosyphilis, congenital syphilis.	General paresis.
Colloidal gold test.	Undiagnosed condition.	General paresis, tabes, etc.
Pleocytosis and albumin.		
Pleocytosis and Wassermann reaction.	- - -	General paresis, cerebrospinal syphilis.
Pleocytosis and colloidal gold test.	- - -	General paresis.
Globulin and albumin.	Cerebrospinal syphilis, trauma, cerebral hemorrhage, brain tumor, chronic alcoholism.	General paresis.
Albumin and Wassermann reaction.		
Wassermann reaction and colloidal gold test.	- - -	General paresis.
Albumin and colloidal gold test.	Undiagnosed mental disease.	Cerebrospinal syphilis.
Pleocytosis, globulin and albumin.		
Pleocytosis, albumin, Wassermann reaction.	Cerebrospinal syphilis.	General paresis.
Pleocytosis, albumin, colloidal gold test.		
Pleocytosis, Wassermann reaction, colloidal gold test.	Neurosyphilis.	
Globulin, albumin and Wassermann reaction.	- - -	General paresis, cerebrospinal syphilis.
Globulin, albumin and colloidal gold test.	Multiple sclerosis.	Tabes, cerebrospinal syphilis.
Albumin, Wassermann reaction and colloidal gold test.		
Pleocytosis, globulin, albumin and Wassermann reaction.		
Pleocytosis, albumin, colloidal gold test and Wassermann reaction.	- - -	General paresis.
Pleocytosis, globulin and colloidal gold test.	Multiple sclerosis, brain tumor, apoplexy.	General paresis.
Globulin, albumin, Wassermann reaction and colloidal gold test.	General paresis, cerebrospinal syphilis.	General paresis.
Pleocytosis, globulin, albumin, Wassermann reaction and colloidal gold test.	General paresis, tabes, cerebrospinal syphilis.	General paresis, tabes, etc.

Pleocytosis is the most variable of the abnormal findings. It is not infrequently absent in the chronic inflammatory processes, *e.g.*, in general paresis, tabes, brain tumor and multiple sclerosis, when the other tests are positive. On the other hand, it may be present in the absence of all other tests. For example, a woman suffering from glycosuria and a mild depression showed 12 cells per cubic millimeter; a second puncture showed 16 cells per cubic millimeter. Her husband was a tabetic. A second example is that of a twenty-year-old boy with all the signs of congenital syphilis, with outbreaks of violence, confusion and amnesia. He showed 56 cells per cubic millimeter, the other spinal fluid reactions being negative.

An increased amount of albumin as the only abnormal finding is not infrequent. In many instances where one finds this as the only evidence of pathology, one is at a loss to be able to interpret it, and we have seen frequent examples of this sort in dementia præcox and unclassified psychoses. According to Myerson an increased amount of albumin is common in Korsakoff's psychosis. I have been able to confirm this in a very small minority of Korsakoff cases. It also occurs after fractured skull and after fairly recent hemorrhage.

The gold reaction may occasionally be found as the only positive test, though this has been quite rare in our experience. We have found it in a few psychotic cases in which we were unable to explain its significance and in a few cases of syphilis.

It seems unnecessary to go into detail as to the combination of these findings with their clinical significance. It suffices to indicate on the table in what conditions we have found these to occur.

In cases of neurosyphilis receiving intensive antisyphilitic treatment, there usually is a change in the laboratory tests. We find that there is no general rule as to which test is the first to become weakened or to disappear, or as to which will remain positive. As one would expect, they do not all change at identically the same time. Thus in cases of general paresis undergoing treatment the Wassermann reaction is frequently unchanged despite long and intensive arsenic and mercury injections, and may remain positive after all other tests have become normal. In another case, with the same diagnosis and similar spinal fluid findings before treatment, the Wassermann reaction may be the first test to become negative. The same variation is to be found with the colloidal gold test, globulin and albumin.

In the table (third column) we have indicated the combination of findings that we have seen in treated neurosyphilitic cases. In addition a few examples are given in more detail.

Report of Cases.

Observation 1. *Wassermann Reaction remained Positive; all Other Tests became Negative.* — Woman, 57 years of age, diagnosed as a case of general paresis.

Before treatment: Wassermann reaction +; globulin + + +; albumin + + +; cells 22 per c.mm.; colloidal gold test, general paresis.

After treatment: Wassermann reaction +; globulin 0; albumin negative; cells 0 per c.mm.; colloidal gold test, negative.

Observation 2. *Colloidal Gold Test remained Positive; all Other Tests became Normal.* — Diagnosis: General paresis.

Before treatment: Wassermann reaction +; globulin + + +; Albumin + + +; cells 37 per c.mm.; colloidal gold test, general paresis.

After treatment: Wassermann reaction —; globulin 0; albumin negative; cells 3 per c.mm.; colloidal gold test, general paresis.

Observation 3. *Pleocytosis and Wassermann Reaction remained Positive; Other Tests Negative.* — The patient was a man of 35 with numerous neurasthenoid complaints, blood and spinal fluid positive to all tests. After two years of treatment spinal fluid findings were: Wassermann reaction +; globulin 0; albumin negative; cells 110 per c.mm.; colloidal gold test negative.

Observation 4. *Globulin and Albumin remained Positive; Other Tests Negative.* — Diagnosis: General paresis.

Before treatment: Wassermann reaction +; globulin + + +; albumin + + +; cells 90 per c.mm.; colloidal gold test 5555553000.

After treatment: Wassermann reaction —; globulin + +; albumin + +; cells 3 per c.mm.; colloidal gold test negative.

Observation 5. *Colloidal Gold Test and Wassermann Reaction remained Positive; Other Tests became Negative.* — Diagnosis: General paresis.

Before treatment: Wassermann reaction +; globulin + + +; albumin + + +; cells 22 per c.mm.; colloidal gold test, general paresis.

After treatment: Wassermann reaction +; globulin 0; albumin negative; cells 0 per c.mm.; colloidal gold test, general paresis.

Observation 6. *Albumin and Colloidal Gold Test remained Positive; Other Tests became Negative.* — Diagnosis: Cerebrospinal syphilis.

Before treatment: Wassermann reaction +; globulin + + +; albumin + + +; cells 11 per c.mm.; colloidal gold test 5432210000.

After treatment: Wassermann reaction negative; globulin 0; albumin +; cells 3 per c.mm.; colloidal gold test 0134310000.

Observation 7. *Globulin, Albumin and Wassermann Reaction remained Positive; Pleocytosis and Colloidal Gold Test became Negative.* — Diagnosis: General paresis.

Before treatment: Wassermann reaction +; globulin + + +; albumin + + +; cells 45 per c.mm.; colloidal gold test 5555555200.

After treatment: Wassermann reaction +; globulin ++; albumin + +; cells 4 per c.mm.; colloidal gold test negative.

Observation 8. *Globulin, Albumin and Colloidal Gold Test remained Positive; Wassermann Reaction and Pleocytosis became Negative.* — Diagnosis: Cerebrospinal syphilis.

Before treatment: Wassermann reaction +; globulin + + +; albumin + + +; cells 56 per c.mm.; colloidal gold test, 0013321000.

After treatment: Wassermann reaction negative, globulin +; albumin +; cells 0 per c.mm.; colloidal gold test 2223310000.

Observation 9. *Wassermann Reaction became Negative; Other Tests remained Positive.* — Diagnosis: Cerebrospinal syphilis.

Before treatment: Wassermann reaction +; globulin + + +; albumin + + + +; cells 41 per c.mm.; colloidal gold test, general paresis.

After treatment: Wassermann reaction —; globulin + +; albumin + +; cells 9 per c.mm.; colloidal gold test, syphilitic.

Observation 10. *Pleocytosis reduced to Normal; Other Tests remained Negative.* — This is a very frequent finding.

Even though not a part of this discussion, we would like to add that the Wassermann reaction in the blood serum varies independently of the spinal fluid findings. Thus it may become negative while all the spinal fluid tests remain unchanged, or it may remain positive when all the spinal fluid tests become negative. It is also pertinent to note that the changes in these spinal fluid tests do not always parallel clinical changes in the patients. Thus we have seen illustrations where although the tests became negative the symptoms were in no way improved; and on the other hand, where there was marked symptomatic improvement without any change in the tests.

Summary.

Of the five spinal fluid laboratory tests commonly used, only cells and albumin are normal constituents of the fluid, and the excess amounts of these are evidence of pathology. The Wassermann reaction is for practical purposes specific for syphilis of the nervous system. Pleocytosis, globulin, albumin and colloidal gold reaction are generally indicative of an inflammatory reaction of brain, cord or meninges. These tests may be positive owing to infection, mechanical injury, tumor, trauma, vascular insults, multiple sclerosis, etc. As a rule, globulin, albumin increase, pleocytosis and a positive colloidal gold reaction occur together,

and when the Wassermann reaction is positive, it is usual for the other four to be positive also. Although usually present together, and in a general way indicative of the same pathologic condition, each reaction is produced by a distinct chemical element which may be present alone (except that theoretically globulin means an increase in the total amount of albumin, as globulin is a special albumin). Thus one may find the Wassermann reaction positive, all other tests negative, a positive colloidal gold reaction as the only positive finding, only a pleocytosis or merely an albumin increase. Further, they may occur in various combinations. This is theoretically possible on the basis of difference in chemical constitution, and it is shown in this paper that this actually does occur.

Additional evidence of the independence of each element is offered in the result of treatment of cases of neurosyphilis. Starting with all tests positive, it is shown that they become negative, often one at a time, and the different combinations are left positive, or only one is left positive.

Conclusions.

1. There is a nonconcomitancy of the inflammatory elements of the spinal fluid commonly tested for in diagnosis of disease of the central nervous system.

2. Any one may be present or absent when the others are present, with the exception that globulin presages an increased amount of albumin.

3. No spinal fluid can be considered negative in which all these tests have not been used.

4. No one element tested for contains the element or fraction that gives another test, except that the total albumin contains the globulin fraction, in part at least.

5. In neurosyphilitic cases receiving treatment these substances disappear at differing rates which vary in different cases, so that no general law can be laid down as to which element is most easily affected by treatment in any particular case, though in general the pleocytosis disappears first.

6. The presence or absence of these products of inflammatory reaction does not always parallel the clinical change in the treated neurosyphilitic patient.

A NOTE ON A CERTAIN ANOMALY OF GYRATION IN BRAINS OF THE INSANE.*

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Influenced by Southard's work on anomalies and scleroses in brains of the insane, especially from cases of dementia præcox, the writer early in his service as pathologist at Danvers began to search for such alterations in all brains coming into his hands.

Attention soon became focused on a frequently occurring anomaly, which at first appeared to be found only in brains from cases of manic-depressive psychosis and dementia præcox.

This anomaly was described in terms of "gyral interruption," and it was only recently learned that the same type of anomaly has been described in terms of continuity of fissures by Benedikt, and described (though not always as anomaly) by many authors, including Retzius, Turner, Schuster and others.

Up to the present, attention has been fixed on the central fissure and the pre-central and post-central gyri. The plan is eventually to extend the study to all gyri through the medium of a series of photographs made under standard conditions of 100 unselected brains.

The anomaly may be described briefly as follows: Normally the central fissure does not connect with any other fissure. It is shut off from the Sylvian fissure by a bar of cortex which connects the pre-central and post-central gyri. The pre-central and post-central gyri are normally continuous, and this effectively prevents other sulci communicating with the central fissure. In the anomalous cases a fissure cuts through either the pre-central or the post-central gyrus, most commonly the former, and runs into the central fissure. I have not, so far, completely analyzed all cases to determine the number in which the central fissure runs into the Sylvian fissure. This note concerns those cases in which an interruption of either pre-central or post-central gyrus occurred.

* No. 66, Danvers State Hospital Papers; contributed to a series in celebration of the tenth anniversary of the Bullard Professorship of Neuropathology, Harvard Medical School.

I have presented in Figs. 1, 2 and 3 some photographs of brains which show the anomaly. Fig. 1 shows a brain in which there were interruptions of both pre-central gyri and in which the central fissure runs into the Sylvian fissure. Fig. 2 shows an interruption of the left pre-central gyrus, the central sulcus communicating with the Sylvian fissure, a less marked interruption of the post-central gyrus, and an interruption of the right pre-central gyrus. Fig. 3 shows an interruption of the left post-central gyrus, this being the only one of four gyri interrupted. This also shows another common finding in this type of case, namely, the tendency to the formation of three or more "ascending" gyri instead of two.

TABLE I. — *Interruptions — 100 Brains.*

DIAGNOSES.	Number of Cases.	With Interruptions.
Paresis,	27	12
Senile dementia,	13	8
Arteriosclerosis,	9	2
Organic,	3	3
Toxic,	8	3
Miscellaneous,	3	0
Dementia præcox,	17	16
Manic depressive,	15	14
Imbecile,	2	2
Paranoia,	1	1
Presenile delusional,	1	1
Epilepsy,	1	1

The material for this study consists of 100 unselected psychotic cases autopsied at Danvers Hospital. After somewhat detailed study in the gross, the brains were photographed when hardened in formalin. The series of photographs for each brain was as follows: The vertex and base were photographed with pia intact; then the pia was stripped and the following photographs made: vertex, base, lateral and mesial surfaces of right and left hemispheres; three plates of sections of the cerebrum; and one plate of sections of the cerebellum. All photographs were made under standard conditions, and the magnification is

the same in each brain for each view. Thus there is a slight difference in the magnification of the vertex and of the hemispheres. This difference is not, however, very great.

In Table I will be found the distribution by diagnosis of the cases autopsied, and the number of cases in each group in which interruption of either pre-central or post-central gyri was observed.

It will be seen that there were 63 cases in the groups that are not necessarily hereditary and having a more or less definite pathology. Among these 63 cases 28 showed interruptions of one or more gyri. I have used this group of cases as my standard of comparison with the groups in which the psychosis might be regarded as inherent or functional, or due to neural instability or lack of development. In other words, I have regarded these cases somewhat in the light of a normal series.

TABLE II. — *Insane Heredity.*

DIAGNOSES.	Insane Heredity (Per Cent).	Unknown.	Negative (Per Cent).
Paresis,	17	–	83
Senile dementia,	–	66	34
Senile dementia plus art,	50	–	50
Arteriosclerotic,	100	–	–
Organic,	33	67	–
Toxic,	33	–	67
Dementia præcox,	42	33	25
Manic depressive,	67	22	11

When we turn to so-called functional psychosis (dementia præcox, etc.), we find that out of 37 cases 35 show the anomaly. In other words, about 44 per cent of the group that might be called organic or extraneous psychoses show the anomaly; practically 95 per cent of the functional or endogenous psychoses show it. In order to determine whether or not the anomaly might be regarded as an evidence of hereditary neural instability, we have investigated the heredity of the cases showing interruptions. These results are presented in Table II.

The facts are somewhat uneven, but they do demonstrate that insane heredity had played an important part in only two groups of cases, namely, the arteriosclerotic and manic-depressive.

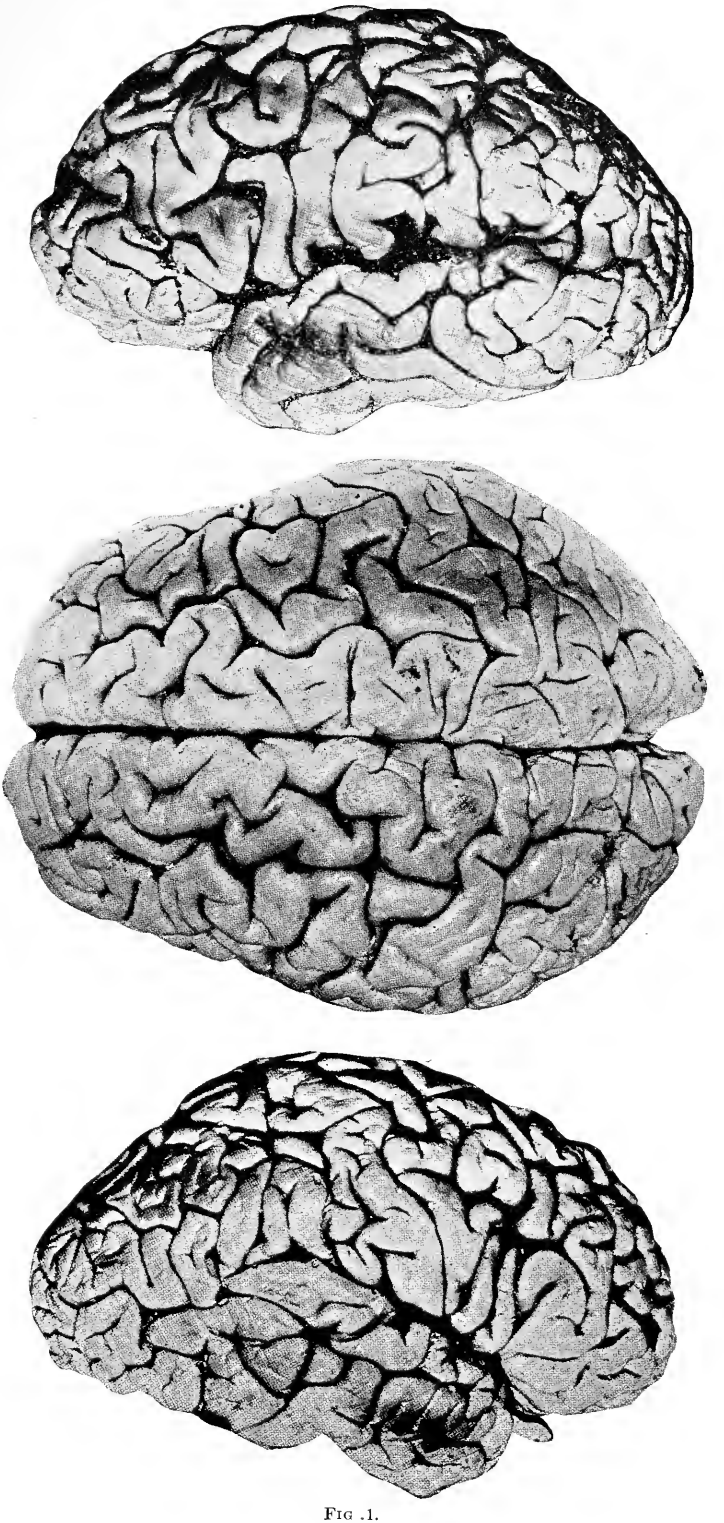

FIG .1.

PLATE II.

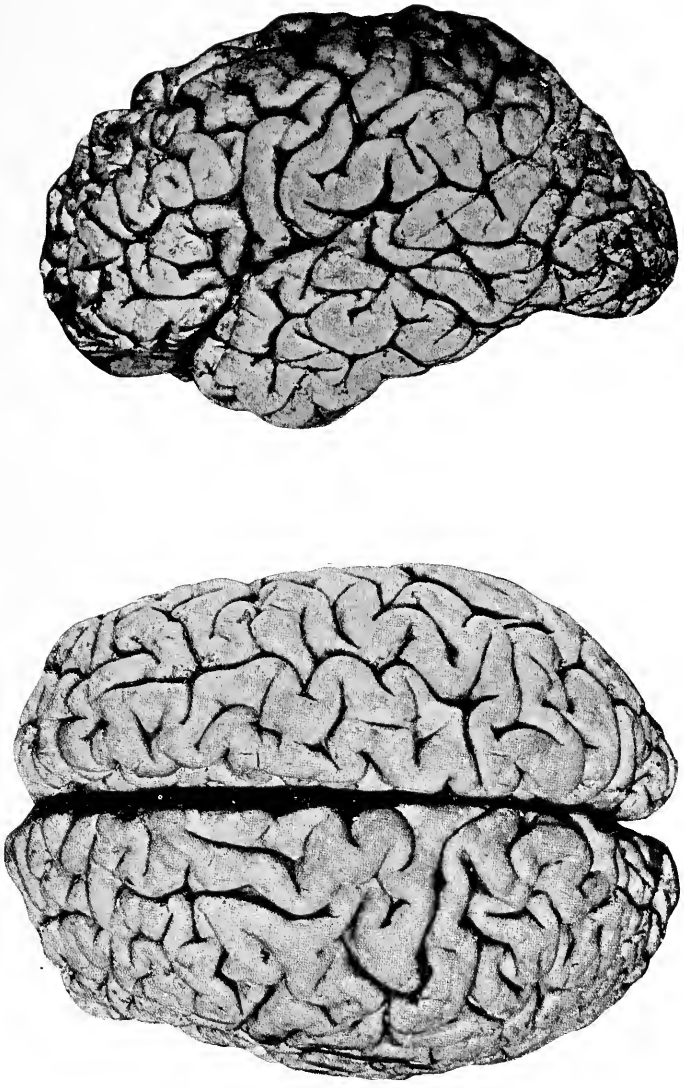

FIG. 2.

PLATE III.

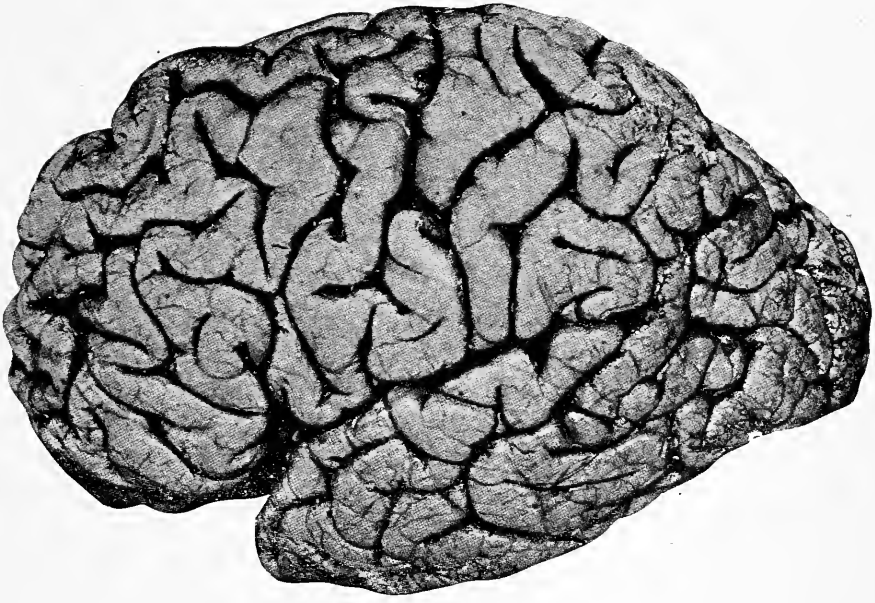

FIG. 3.

The importance of this anomaly is thought to be as follows: the fact that it does occur is some evidence of a loosely organized nervous system. The anomaly is easy to find, and serves as an index of the organization of the brain, and I believe that careful study of this and similar anomalies represents a step in advance in the cerebral pathology of the mental diseases. I do not, of course, believe that it has any direct or causal relationship to the symptoms of the psychosis.

THE LEUKOCYTIC REACTION IN A PARATYPHOID DYSENTERY AND FOLLOWING VACCINE INOCULATIONS.*

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The occasion of this report was a dysentery which appeared as an epidemic [1] in 1915 in the Boston State Hospital. The organism which caused the disease belonged to the paratyphoid enteritidis group, but could not be identified with any of the well-known members. Clinically, the disease appeared in three forms, — a dysenteric-pneumonic, a dysenteric and a diarrheal. The duration of the disease was from five days to three weeks. The majority of the cases occurred among the old and feeble women patients in the infirmary department.

The 22 blood examinations in the table (I) represent 12 severe cases. The blood picture varied somewhat in different patients and in the same patient during the course of the disease. The total white counts were between 5,100 and 13,300. The differential count was not quite so variable as the total count, in that it remained more constant to the form of the disease. The per cent of polynuclears was relatively higher and that of the lymphocytes lower in the pneumonic than in the pure dysenteric form. In the dysenteric cases uncomplicated with pneumonia, the lymphocytes persisted rather high during the first two weeks, — between 27 and 40 per cent; in two recovered pneumonic cases the lymphocytes showed a high per cent in the third week during convalescence, — 37 and 43 per cent. A count made in one case of an acute arthritis following a short severe attack of dysentery resembled the pneumonic cases. Eosinophiles were not found in any case during the first week; in the second week they reappeared in 5 to 2 per cent. Transitionals gave a higher per cent in the first than in the second week. In all cases blood platelets were much increased throughout the disease and in early convalescence. There was no evidence of an anemia, judging from the hemoglobin per cent and the character of the red blood cells.

Reports of blood examinations in paratyphoid infections have not been numerous, but a review of them shows either a normal

* This is one of a series of fifteen papers (269, 1919.12) offered to Prof. E. E. Southard in honor of the decennium of the Bullard Professorship of Neuropathology, Harvard Medical School.

picture or changes in the white blood cells similar to those in typhoid fever. Uhlenroth and Hubener [2] state that there may be a leukopenia in the typhoid form of a paratyphoid B infection, with an early loss of eosinophiles and a late relative increase in lymphocytes, quite like a true typhoid. In a paratyphoid A [3]

TABLE I. — *The Leukocytes in a Paratyphoid Dysentery.*

CASE.	Day.	Total.	Poly.	Lymph.	Trans. L. M.	Eosin.	Bas.	Remarks.
R. W., . .	1	6,400	66	29	4.75	–	.25	T. 104.8°.
M. G., . .	2	6,400	56	29	15	–	–	T. 102.8°.
E. O'M., . .	3	13,100	68	31	1	–	–	Pneumonic.
E. O'B., . .	3	5,400	59	27	14	–	–	– –
A. S., . .	4	5,100	77	13	10	–	–	Pneumonic. Death 5th day.
M. C., . .	4	–	54	40	6	–	–	– –
E. O'B., . .	5	–	59	33	8	–	–	– –
M. C., . .	6	12,800	66	30	4	–	–	– –
E. M'K., . .	6	12,200	76	10	14	–	–	Pneumonic.
M. P., . .	7	–	72	19	8	–	–	Pneumonic. Death 11th day.
M. W., . .	8	–	53	41	4.5	.5	–	– –
J. C., . .	9	–	80	13	2	.5	–	Pneumonic.
J. M., . .	10	8,800	63	25	6	2	1	Convalescent.
M. G., . .	13	–	64.5	30	5	.5	–	– –
M. C., . .	14	10,000	62	34	3	–	1	– –
E. O'B., . .	15	8,000	65	31	3	.5	–	Convalescent.
E. M'K., . .	17	–	59	37	3.5	.5	–	Protracted case.
E. O'B., . .	18	–	65	26	2	7	–	Convalescent.
T. S., . .	18	10,000	71	23.5	3.5	1.5	.5	T. 101°. Acute arthritis.
M. W., . .	18	–	63	33	1	3	–	Convalescent.
J. C., . .	19	–	52	43	4	.5	–	Convalescent.
M. G., . .	23	8,200	65.5	25	9	.5	–	Convalescent.

infection of typhoid form in this hospital in 1910, blood examinations showed total leukocyte counts between 3,200 and 8,000, with the lowest count on the fourth day. The lymphocytes showed a relative increase on the fourth day, and the eosinophiles, although not entirely disappearing, were reduced on the third day. Rolly,[4] in 1911, reported total leukocyte counts made in about 35 cases of paratyphoid A and B infections of the para-

typhoid form. In the B infections the counts were between 3,000 and 7,000, not apparently decreasing with the progress of the disease. In one case of paratyphoid A infection, six counts made between the twelfth and the twenty-second day fluctuated between 3,800 and 6,400. One of the cases of paratyphoid B is of interest in the light of our findings. This patient had a double pneumonia on the thirteenth day, with a count of 17,000, falling to 6,200 on the twenty-fourth day, with an improvement in the lung condition. Rolly questioned whether the pneumonia may not have been due to a mixed infection. Hall and Adam [5] in the present European war have studied blood smears from soldiers convalescent from dysenteries, typhoid fever and paratyphoid A and B infections. They observed a relative lymphocytosis with a low polynuclear per cent following both typhoid fever and a paratyphoid A infection up to the thirteenth week. The fact that from the Mediterranean area all convalescents from a paratyphoid A infection showed a normally high polynuclear per cent indicated to the writers that these patients may have suffered from another form of dysentery, amœbic or bacillary, at the same time. They did not explain the normal polynuclear per cent found in all convalescents from a paratyphoid B infection, nor did they mention the clinical form of the disease. Ordway,[6] in an experimental study of rabbits suffering from a typhoid-like disease caused by the bacillus suipestifer, observed that the total white blood counts were not altered by the infection.

In this epidemic dysentery the one persistent similarity to a typhoid picture was the loss of eosinophiles during the first week. It is probable that the increase in polynuclears in some cases was related to the pneumonic process. In two septicemic pneumonic cases that came to autopsy, the paratyphoid bacillus was found in the lung lesions associated with a streptococcus in one case and a staphylococcus in the other. We have not sufficient data to say whether higher counts are more usual in a dysenteric than in a typhoid form of a paratyphoid infection.

The Leukocytic Reaction following Vaccine Inoculations.

Gay and Claypole [7] in their experiments in typhoid immunization found that a specific hyperleukocytosis, preceded by a leukopenia was produced in typhoid immune rabbits by inoculations with typhoid vaccine, and that the increase in cells was due to the polymorphonuclear. The leukocytic response was more rapid and rose to a greater height in the immunized rabbit

than in the normal animal. H. I. McWilliams,[8] in a more recent report of similar experiments with rabbits, noted a hyperleukocytosis which was not of a higher grade in the immune than in the non-immune animal.

Both Gay[9] and McWilliams[10] have described the leukocytic reaction following injections of vaccine in typhoid fever. A chill and rise in temperature are coincident with a leukopenia shortly after the inoculation, and a few hours later, with the lowering of the temperature and a lessening of symptoms, there is a high-grade hyperleukocytosis. The relation of the hyperleukocytosis or "leukocytic crisis" to the freeing of the antibodies indicates the possible value of these studies in vaccine therapy and prophylactic immunization. Although the blood examinations in this paratyphoid dysentery have been limited to human cases, and have not the exactness of results obtained in animal experimentation, they have a certain clinical value because it has been possible to observe these cases over a number of months.

A polymorphonuclear leukocytosis, both actual and relative, was demonstrated in one protracted case (M. G.) during the first outbreak of dysentery after a repeated therapeutic dose of the dysenteric vaccine. Six hours after a subcutaneous injection of 75,000,000, the total count rose from 6,400 to 19,400 and the polymorphonuclears from 56 to 76 per cent, with a loss of eosinophiles. No constitutional reaction followed successive small doses in this patient, although there was an apparent improvement in symptoms.

A polymorphonuclear leukocytosis was observed in a second case eighteen hours after an initial prophylactic inoculation of 500,000,000, and six hours after the onset of a severe constitutional reaction with fever and vomiting. Total count, 18,800; polymorphonuclears, .92; lymphocytes, .08; large mononuclears, transitionals and eosinophiles, 0. This was the only count made in this case. There is no record eleven months later that this patient has had an attack of the disease.

Because of these isolated observations it seemed worth while to study the leukocytic reaction more carefully, and during the seventeen months following the first outbreak of the disease several series of examinations were made, including one woman and four men who had neither the disease nor prophylactic treatment, and four women who had had the disease from nine to seventeen months previously (Tables II and III). Subcutaneous injections of vaccine were given for two or three successive weeks in doses as in prophylactic treatment, beginning

with 500,000,000. In two cases the counts were taken at two-hour intervals during the first twenty-six hours after the inoculation. In all the other cases counts were taken either during the first twelve or second twelve hours at one-half, one hour, or two-hour intervals.* Differential as well as total counts were made and a control count was made in each case. There was no constitutional reaction observed in any of these cases, and the local reaction was a moderate one.

TABLE II. — *Leukocytic Reaction following Vaccine Inoculations in those who have had the Disease.*

Case J. W. — Dysentery 11 months previously.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	6,300	56	36.5	4.5	1.5	1.5
Hours after Inoculation.						
12,	9,100	–	–	–	–	–
14,	10,000	70	25	5	–	–
15¾,	10,400	70	25	2.5	1	1.5
18,	7,200	61	35	3.5	.5	–
20,	6,800	56	43	1	–	–

Case J. W. — Dysentery 11 months previously, seven days after first inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	7,300	57.5	31.5	8	2	1
Hours after Inoculation.						
12,	11,400	61	30	8	1	–
14,	11,300	75.5	18.5	5	1	–
16,	10,600	–	–	–	–	–
18,	10,600	76	18	6	–	–
20,	10,200	59.5	40	–	.5	–

* A number of these counts were made by Mr. John C. Rock of the Harvard Medical School

TABLE II. — *Leukocytic Reaction following Vaccine Inoculations in those who have had the Disease* — Continued.

Case J. W. — Dysentery 11 months previously, eighteen days after second inoculation.

[Vaccine 1,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Mast.
Control, ...	9,100	38.5	56.5	2.5	1.5	1
Hours after Inoculation.						
12¼, ...	4,600	68	27.5	2.5	1	1
13¼, ...	9,900	64.5	25.5	6	2	–
14¼, ...	9,400	63	32	3	2	–
15¼, ...	17,300	68	28	3	1	–
17¼, ...	10,800	64	32	3.5	.5	–
19¼, ...	11,500	63	36.5	.5	–	–
21½, ...	11,900	69	30	–	1	–
23½, ...	9,900	63	33.5	2.5	1	–

Case A. O. — Twelve months after first attack, second day after recovery from second attack.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control, ...	7,400	–	–	–	–	–
Hours after Inoculation.						
12¼, ...	12,200	–	–	–	–	–
13¼, ...	14,500	–	–	–	–	–
14¼, ...	15,200	76	19	4	.5	.5
15¼, ...	19,500	72	20	2.5	5	.5
17¼, ...	22,700	71.5	20.5	1.5	4.5	2
19¼, ...	13,600	71	22.5	4	2.5	–
21½, ...	17,300	60	35	2.5	2.5	–
23½, ...	10,000	45	47.5	4	3.5	–

TABLE II. — *Leukocytic Reaction following Vaccine Inoculations in those who have had the Disease* — Continued.

Case A. O. — Eighth day after first inoculation, tenth day after recovery from second attack.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	7,000	42	45	5.5	6	1.5
Hours after Inoculation.						
14,	9,100	58	37.5	1	3.5	–
15,	9,600	65	33	2	–	–
16,	7,800	59.5	34	4	2	.5
17,	7,400	62	33	1.5	3.5	–
18,	7,300	66.5	29	2.5	1	1
19,	8,500	73	24	2	1	0
20,	8,900	73	24	0	2	1
21,	10,700	78	19	1	2	0
22,	11,300	71	26	1	2	0

Case M. G. — Dysentery nine months previously.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.	Temp.
Control,	7,800	60	35	3	2	–	98.6
Hours after Inoculation.							
2,	8,600	72	20.5	5.5	2	–	98
4,	8,200	–	–	–	–	–	98
6,	6,800	56.5	34.5	7	2	–	98.4
8,	9,800	69.5	25	4	1.5	–	98.2
10,	13,300	66	28.5	4	1.5	–	98.8
12,	15,500	54.5	36.5	8	1	–	98.8
14,	13,900	64	30	6	0	.5	98
16,	11,700	64	35.5	.5	0	–	98
18,	9,300	71	25	3	1	–	98
20,	10,600	73.5	20	5	1.5	–	97
22,	10,600	76	22	2	0	–	98.2
24,	9,000	63	31	6	0	–	98.4
26,	9,000	78	22	0	0	–	99.4

TABLE II. — *Leukocytic Reaction following Vaccine Inoculations in those who have had the Disease* — Continued.

Case M. G. — Third day recurrent attack, 17 months after first attack.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	9,900	60	34.5	5	.5	–
Hours after Inoculation.						
½	13,200	59.5	37.5	2	1	–
1,	10,700	61	34.5	2.5	2	–
1½,	9,800	67.25	28.5	4.25	–	–
2,	7,600	44	54	2	–	–
3,	7,800	66	32	–	2	–
19½,	7,100	80	20	0	0	0
20½,	10,400	70	26	2	1	1
21¼,	11,000	71	26	2	1	0
22¼,	10,700	81	19	–	0	0
23¼,	9,600	73	26	1	0	0
24¼,	13,700	71	29	0	0	0

Case M. C. — Sixteen months after first attack.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	12,700	57	40	0	3	0
Hours after Inoculation.						
2½,	8,400	68	26	0	5	1
3,	10,400	67	29	0	3	1
6,	10,100	52	44	0	4	0
8,	10,700	50	48	1	1	–
10,	11,600	62	37	0	1	0
11,	11,400	65	47	0	1	0
12,	10,500	60	34	3.5	2.5	–

TABLE II. — *Leukocytic Reaction following Vaccine Inoculations in those who have had the Disease* — Continued.

Case M. C. — Seven days after first inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	12,400	–	–	–	–	–
Hours after Inoculation.						
2,	9,600	56	39	1	4	–
4,	14,200	58	33	3	5	1
6,	9,200	58	31	4	6	1
9,	12,000	54	41	3	2	–
11,	14,000	40	55	4	1	–

Case M. C. — Nine days after second inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	9,100	49	50	.5	.5	–
Hours after Inoculation.						
2,	12,500	68	28	1	3	–
3,	11,500	56	42	1	1	–
5,	15,100	75	25	0	0	–
6,	14,600	60	40	0	0	–
7¼,	14,300	70	30	0	0	–
8¼,	13,700	60	40	0	0	–
10,	11,900	74	25	0	1	–

TABLE II. — *Leukocytic Reaction following Vaccine Inoculations in those who have had the Disease* — Concluded.

Case M. C. — One month after vaccination, second day after recovery from recurrent attack.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	13,900	50	39	10	1	–
Hours after Inoculation.						
½,	12,200	49	45	4	2	–
1,	7,400	56	40	2	2	–
1½,	6,200	49	44.5	2.5	4	–
2,	9,600	79	21	0	9	–
3,	9,700	51	41.5	5	2.5	–
19,	8,200	64	27.5	8	.5	–
20,	9,000	76	19.5	.5	4	–
20¾,	8,300	63	34	2	1	–
21,	11,200	66	31.5	1	.5	–
22,	9,900	–	–	–	–	–
23,	12,500	77	18.5	3	1.25	.25

TABLE III. — *The Leukocytic Reaction in Prophylactic Treatment.*

Case W. F. — Prophylactic treatment.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Mast.
Control,	11,600	64	29	1	6	–
Hours after Inoculation.						
2,	9,400	67.5	28	0	4.5	0
4,	10,300	59	35.5	1	4	.5
6,	9,300	59	33	1	6	1
8¼,	9,500	67	29	0	4	0
10¼,	10,800	70.5	25	1	3	.5
22½,	12,700	64	30	2	3	1
24½,	12,000	69	29	1	1	–

TABLE III. — *The Leukocytic Reaction in Prophylactic Treatment* — Continued.

Case W. F. — Second inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	9,200	67	21	8	4	–
Hours after Inoculation.						
2,	11,000	69.5	24.5	3.5	2.5	–
4,	14,400	73.5	20.5	5.5	.5	–
6¼,	13,300	74	17.5	2.5	5.5	.5
9½,	15,400	73.5	21.5	2.5	2.5	–
11½,	16,500	78	14	4	4	–

Case W. F. — Third inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	10,000	69	28.5	1	1.5	–
Hours after Inoculation.						
2,	11,500	74	20	2.5	3.5	–
3,	7,800	60.5	33	2	4.5	–
5,	12,900	78	18	1	3	–
6,	13,000	69	21.5	4	5	.5
7,	12,600	69	27	–	4	–
8,	13,000	75	21	–	4	–
10,	13,300	64	32	1	3	–

TABLE III. — *The Leukocytic Reaction in Prophylactic Treatment* — Continued.

Case C. H. — Prophylactic treatment.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.	Temp.
Control,	5,100	42	47.5	7.5	3	–	98
Hours after Inoculation.							
2,	6,800	51	37.5	8	.5	3	98.6
4,	7,200	45	47	5	–	3	98.8
6,	9,400	70.5	25	4	.5	–	99
8,	9,400	66	25	6	2.5	.5	98.8
10,	10,800	62	29.5	6	2	.5	99
12,	12,900	59	29.5	6.5	3	2	99
14,	10,400	57	32	8	1	2	98
16,	7,800	56	36	5	2	1	98
18,	6,800	53	41	5	1	–	97.6
20,	7,200	48	43	7	1	1	97.2
22,	6,400	49	40	9	1	1	99
24,	7,500	58	29	12	1	–	99
26,	6,800	50	44	5	–	–	99

Case S. S. — *Prophylactic treatment.*

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	5,400	63	26	6	5	–
Hours after Inoculation.						
12,	8,400	62	29	7	2	–
14,	11,400	63.5	30	–	5	1.5
16,	10,900	56	36	3	4	1
18,	12,400	51	40	5	3	1

TABLE III. — *The Leukocytic Reaction in Prophylactic Treatment* — Continued.

Case S. S. — Second inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control,	9,400	53	42	3	1.5	.5
Hours after Inoculation.						
12,	19,500	62.5	35.5	1	1	–
14,	14,800	50	42.5	3	4	.5
16,	13,200	72	24	2	2	–
18,	20,200	73	22	2	3	–
20,	16,000	64.5	31	3	1.5	–

Case F. N. — Prophylactic treatment. First inoculation.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Mast.
Control,	12,400	69	27	1	3	–
Hours after Inoculation.						
2,	14,000	73	23	3	1	–
4,	11,300	67	29	–	4	–
6,	10,200	74	19	2	5	–
8,	10,200	78	14	2.5	5	.5
10,	12,000	60.5	32	2	5	.5
22,	14,600	–	–	–	–	–
24,	13,000	–	–	–	–	–

Case F. N. — Prophylactic treatment. Second inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Mast.
Control,	12,200	–	–	–	–	–
Hours after Inoculation.						
2,	14,500	80	15 5	3	1 5	–
4¼,	23,000	72	21 5	1	4 5	1
6¼,	24,000	69	27	1	2	1
8¾,	19,400	79	17	1	3	–
10¾,	16,000	63	30	2	5	–

TABLE III. — *The Leukocytic Reaction in Prophylactic Treatment* — Concluded.

Case H. D. — Prophylactic treatment.

[Vaccine 500,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control, ...	6,600	49	46	1	4	–
Hours after Inoculation.						
12, ...	10,400	61	29	5	5	–
14, ...	10,800	69	22	2	7	–
16, ...	11,500	77	19	1	3	–
18, ...	13,000	60	34	3	3	–
20, ...	9,900	58	36	1	5	–

Case H. D. — Second inoculation.

[Vaccine 1,000,000,000.]

TIME.	Total.	% Poly.	% Lymph.	% Trans. L. M.	% Eosin.	% Bas.
Control, ...	8,000	–	–	–	–	–
Hours after Inoculation.						
12, ...	13,200	66	28	5	1	–
14, ...	13,500	75	20	2	3	–
16, ...	14,300	77	20	2	1	–
18, ...	11,500	62	36	2	–	–
20, ...	14,200	59	38	1	2	–

The leukocytic reaction consisted of a hyperleukocytosis, with the highest count rising but little above twice that of the normal count for the individual, and a relative increase in polynuclears at one or more periods during the following twenty-four hours, this relative increase not always being synchronous with the highest total count.

The reaction was somewhat more marked after the second or third inoculation than after the first, except in one case (A. O.), in which the vaccine was injected shortly after a recurrent attack. In this case the reaction was greater after the first injection of 500,000,000 two days after the attack than after the second inoculation of 1,000,000,000, seven days later. One case (M. G.), referred to above as showing marked reaction to vaccine therapy in the first attack, showed a moderate reaction both in total and differential counts following an inoculation of 500,000,000 nine

months later; and on the third day of a recurrent attack seventeen months later gave evidence of a reaction only in a relative increase in polymorphonuclears following an injection of 500,000,000. The diarrhea in this last instance ceased a few hours after the inoculation, and there was no evident constitutional disturbance. The recurrent attacks were milder than the first one, and appeared usually in the form of a diarrhea.

There is no record that the individuals chosen as normal cases in this series of examinations have had an attack of dysentery or diarrhea.

In comparing the leukocytic reaction with the clinical history in these cases the following conclusions have been made: —

1. The stronger normal individuals show more reaction to subcutaneous injections of vaccine than the weaker ones who have had the disease and recurrent attacks.

2. The leukocytic reaction for the individual is more marked during or immediately after an attack of the disease and diminishes with recurrent attacks. This corresponds to the clinical observation that the resistance of the individual to the disease is lessened by a previous attack.

3. The fact that there may be a polymorphonuclear reaction to a subcutaneous injection of vaccine, coincident with the cessation of a diarrhea, would indicate the use of a vaccine therapy. In the few cases in which this treatment has been given the results have been favorable for a recovery from an attack.

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NEWER CONCEPTIONS OF DEMENTIA PRÆCOX BASED ON UNRECOGNIZED WORK.*

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Just as our knowledge of any given subject comes to being out of many little nebulous masses, so we have gained a certain amount of insight into the nature of dementia præcox. And as the science of any subject owes its accurate development to the work of the laboratory, so our present knowledge of dementia præcox has been built up from the many little nebulous masses which have developed in the laboratory, but which have developed into a concrete whole — paradoxical as the idea may seem. And yet, this disease form which makes up nearly a quarter of all the cases admitted to hospitals for the insane, and which accounts, more than any other single factor, for the necessity of building more of such institutions, has been neglected from the only side which can possibly give us hope of combating its spread, — the laboratory side. Its treatment has been largely custodial, symptomatic, not to forget recent developments in industrial teaching and in social service work.

Laboratories deal with technical methods, and for this reason a discussion of our present knowledge of dementia præcox, or a presentation of newer conceptions of dementia præcox from the laboratory point of view, must be more or less intimately linked with a discussion of the methods used in obtaining the knowledge.

The institution of exact methods begins with the investigation of the cause of death by means of the post-mortem examination. The earliest investigation of a case of dementia præcox that I have been able to find, where the brain and organs were examined and the examination published, was in 1844, by Alquié (quoted by Cramer [1] in 1896). The chief finding of interest to us is that the gray matter of the brain was injected. This observation I take to be of the utmost importance, not only because it was a true observation, doubtless, but because it is a frequent finding even to-day, though not confined to dementia præcox, of course. The method of observation is also important and the one most generally used in medicine. It is called the gross method or the macroscopic examination. Using this

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method, much valuable information has been obtained concerning the nature of dementia præcox.

Jehn,[2] in 1877, speaking of acute delirium, and some of these cases certainly look like dementia præcox mentally, remarks on a high grade of vascularity found, as did Alquié. There is hyperemia, clouding of the pia, reddening of the cortex, increased cerebrospinal fluid, and edema of the brain. There are changes in the other organs, and the hemoglobin comes out of the blood. L. Meyer (1857), speaking of "acute fatal hysteria", mentions extensive venous hyperemia (Cramer [1]). Pauly [3] (1869), in a dissertation at Bonn, mentions edema resulting from hyperemia. Schüle [4] (1879) separates two types of acute delirium, — one showing hyperemia of the pia, a few with serous edema, especially of the frontal lobes, some with milky, diffuse or punctiform clouding and reddening of the cortical surface of the meninges; the other group showing nothing in the meninges but a venous hyperemia in the brain and an increase in the cerebrospinal and ventricular fluid. Rezzonico [5] (1884) gives the history of a male of forty-seven years of age who died after eleven days of excitement. There were no external signs of disease or injury, but the cortex and white matter were remarkably hyperemic. Similar observations were made by Ball [6] (1885) and Holsti [7] (1884). Thickening of the meninges without exudate is frequently seen, as noted by Klippel and Lhermitte (quoted by Zingerle [8]), Obregia,[9] Schütz [10] (1909), Lukacs [11] (1908), Marchand,[12] Goldstein [13] and Weber [14] (1899). So hyperemia of the brain, thickening and adhesions of the meninges were the observations of the day in cases which we can recognize to-day as being those of dementia præcox and of the infections or intoxications, and these findings were linked with the interests of the day such as intracranial circulation, pressure and stasis. Such were also the findings of Kahlbaum [15] in his monumental work differentiating katatonia, or tension insanity, as he called it.

The gross method was not exhausted with these observations, but turned in new directions after many years. Examination of the convolutions came next, with the claim that there was atrophy (Klippel and Lhermitte,[16] 1907), that there was decrease in size of the white matter and of the cortex (Obregia, 1906, and Zimmermann,[17] 1907), that there was hemiatrophy and lobar atrophy of the cerebellum (French writers and later Morse and Taft [18]), and that there was convolutional asymmetry (Mondio, quoted by Omorokow [19]).

Another form which the gross method took was the investigation of the relation existing between brain weight and cranial capacity. This was first made practicable by Reichardt [20] (1907-11), who showed that there was little difference between the weight of the brain and the capacity of the cranium in certain cases of katatonia, dying suddenly, with or without convulsions. The same was true in some cases of epilepsy, the difference being 0 per cent. Cases described by Nonne [21] as "pseudotumor cerebri" (1904) are of the same sort, and their histology has been described in detail by Rosental [22] (1911). These are cases which give evidence of tumor clinically, but prove the diagnosis to be wrong by cure or autopsy. Such a case was published by Dreyfus [23] (1907) from the Basle Psychiatric Clinic. The patient was a male dementia præcox of twenty-nine at onset, who died suddenly at thirty-two years of age. The brain was stained with several stains, in sections taken from eight different areas, and no changes were found, but the cord was large for the spinal canal, and the brain was 140 grams too heavy for the cranial capacity. Death was due to acute brain swelling.

The interval between these two great periods of research with the gross methods was taken up with the study of the minute details of brain pathology by means of the microscope and the newly discovered color chemistry. Most of the work on dementia præcox, as in other branches of pathology, has been done with the methods of finer histology, neglecting the more logical ones of photographing the gross changes observed so that they might be preserved for comparison in large numbers of cases from all parts of the world; neglecting the fact that study of the frontal section in series might yield something, and this to be photographed; neglecting the fact that the whole brain microtome can give valuable information in the psychoses, and going directly to the finer histology with the attempt to get the section ever thinner.

The results obtained over the years have been very much at variance, and often appeared to be extremely contradictory, but the time has come when a certain uniformity can be put upon them and they can be understood.

To unify the large amount of material which has accumulated, and at the same time to show that the changes found are very much alike, I have selected cases from the following groups, and have arranged the results under the dementia præcox group, the confusional and delirious group, a single case of "pseudotumor," and the general work on the nervous elements in the psychoses.

In 1896 the findings in the acute case of the paranoia group were given by Cramer.[1] A male of twenty-four, duration seven days, had shown albumin and fatty casts. Temperature was 40.5° C., pulse 132, respiration 48. Autopsy was performed ten hours post mortem. No leucocytes were found in the tissues. There was hemorrhage about the small vessels of the brain and thinning of the interradiary and tangential fibers in places. The writer concludes that a case not manic or melancholic, but paranoiac or possibly confusional, can show severe changes of a non-infectious character. This is the type of case we meet repeatedly in the literature, until we come to agree with Goldstein [24] (1910), that there are few uncomplicated cases in the literature; and we must finally agree that there can be no uncomplicated cases, if our methods of diagnosis and of pathological examination are adequate. Certain it is that the number of supposed uncomplicated cases has become remarkably few with rapid advances in accurate diagnosis and accurate protocol taking.

In 1906 Klippel and Lhermitte [25] described changes in the spinal cord of cases of dementia præcox. One case was that of a male of twenty-nine in which the cord showed changes in the posterior columns exactly like those seen in tabes. Another case, age thirty-five, gave changes in the lateral columns, without meningitis and without cord symptoms clinically. One of these writers [26] had previously (1904) described cases of dementia præcox in which there were no changes in the vascular connective tissue elements of the brain, but only in the neuroepithelial elements. There were no leucocytes, no diapedesis, no hyperemia, no proliferation or degeneration of the walls of the vessels He concluded from his studies that dementia præcox was a degenerative disease of the neuroepithelial elements of the brain and cord without involvement of the vascular connective tissue elements, and that where the latter appeared to be involved the involvement was due to intercurrent disease. In 1909 Moriyasu [26] presented nine cases, studied *in extenso*, in which he showed that the fibrils were fragmented and distinctly decreased in number. Changes in the ganglion cells were definite and distinct, but, in accord with all workers, the changes in the ganglion cells were not characteristic of dementia præcox. Vascular changes were not significant. The glia nuclei were increased about the blood vessels, especially in the white matter, and there was satellitosis about the pyramidal cells. He also says that changes in Clarke's column of cells in the spinal cord

are constant. No plasma cells were found in any of his cases. He studied seven females and two males, ranging in age from twenty-five to fifty-three. The duration of the disease was from a few days in one case to two years in one case. One died of erysipelas, two died suddenly, cause not given, and the cause of death was not given in the other six cases. To have quoted one thorough worker is to have quoted the rest most completely. Klippel and Lhermitte mention a pigment increase in the neuroglia (quoted by Moriyasu [27]). Mondio [28] (1905) says that the changes in the ganglion cells are those seen by others in idiocy and in the intoxications. Obregia [29] mentions chromatolysis and meningeal thickening, with proliferation of the cells of the meninges and of the vascular adventitia.

Glia increase, both cellular and fibrillar, with changes in the cells and fibrils; pigmentation of the nerve cells and of the glia and pigment lying free in the tissues or about the vessels or in the vessel walls or lumen; the presence of small lymphocytes or of leucocytes; loss of myelinated fibers; degeneration products such as fatty and protogonoid granules; satellitosis and neuronophagia have all been observed and recorded.

What are the microscopic findings in the frankly delirious cases? The confusional cases? The toxic cases? Perhaps the first good description of that picture is the one given by Jehn [2] in 1877. The vessels showed fatty degeneration and nuclear heaps and pigmentation. There was extravasation of blood and overgrowth of glia. The lymph spaces contained fat, and the cell protoplasm showed it also. Next, Rezzonico,[5] in 1884, showed dilatation of the finest vessels, with fatty degeneration of their walls and emboli made up of groups of micrococci. He noted in his writings that Briand had already, in 1882, found bacilli in the blood in 3 out of 7 cases of acute delirium. What threw many cases out of the delirious group and into the dementia præcox group, or what corresponded to it then as to-day, was the absence of any notable fever; and albuminuria was only slight. How many times have we seen that ourselves in cases that went rapidly to a fatal termination?

Next, as might be expected, a specific bacillus was described for acute delirium (Bianchi and Piccinio,[30] 1895). But the histological changes found were the same as those found in dementia præcox, — clouding of the pia, edema of the brain, adhesions of the meninges, capillary hemorrhages, extravasation of blood pigment, emigration of leukocytes, acute cellular degeneration

(Cramer, quoted by Binswanger and Berger,[31] 1901), increase of glia and vascular nuclei (Popoff, quoted [31]), swelling and degeneration of the myelin sheath (Schukowsky, quoted [31]), satellitosis, chromatolysis (Weber,[32] 1904).

What were the general findings in the psychoses by Nissl and Alzheimer, and those working at about their time, in and out of their laboratories? Alzheimer,[33] in 1906, remarks that with the same tinctorial methods which enabled us to differentiate general paralysis from senile dementia, etc., we are unable to show differences in the simple psychoses. Pathological changes are not lacking, he states, but who will number the cells or fibers lost? This seems to be his idea of the proper direction for future research in the psychoses. Fat occurs in epilepsy and in many other conditions besides the infections and dementia præcox. Protogonoid substances occur also in amaurotic idiocy (Alzheimer [33]). The neurofibrils, as studied by the Bielschowsky method (Schütz,[34] Jena, 1908), have lost their network arrangement in the cell bodies in dementia præcox, general paralysis and secondary dementia. Glia proliferation has been observed in general paralysis, senile dementia, alcoholics, uremic psychosis and typhus delirium (Nissl, quoted by Alzheimer [35]). Yellow pigment in the cell bodies, first claimed by Campbell [36] to be pathognomonic of senile dementia, was found by Alzheimer [35] to exist also in epilepsy, arteriosclerotic degenerations and in general paralysis. Then Rosental [37] (1913) demonstrated that changes in the glia resembling the ameboid glia could be produced experimentally by the injection into rabbits of guanidin, sodium oxalate or of foreign serum into a sensitized animal. Granular degeneration and neuronophagia were also produced. This writer demonstrated, also, that the ameboid glia were certainly not post-mortem appearances. A series of non-insane cases studied by Vogt [38] (1901) showed degeneration of cells, increase in neuroglia, and exudate in non-insane cases. Tuberculosis, according to him, shows chronic changes in the nerve cells generally, and may show increase in the glia.

With the case of pseudotumor cerebri (Rosental,[22] 1911) there appeared the acute Nissl reaction so often seen in the infectious processes, and also ameboid glia, satellitosis, protogonoid granules, and lipoid inclusions in the cells, just as we have seen in all the conditions presented in this paper.

The earliest and, perhaps, the best statement of the meaning of all this is one written in 1898 by Juliusberger and Meyer.[39]

They were of the opinion that the changes found were "evidence of abnormal life processes in the cell", and this simple statement can scarcely be excelled to-day. We can add just one thing to it, perhaps, and that is to state a little more clearly just what those abnormal life processes are, and just a little as to how they may be effected. We have done this when we consider the reactions of the human organism, with its fats, carbohydrates and proteins, to the foreign substances which invade it, whether or not as bacterial protein or fat, and when we add to our considerations the susceptibility of the individual, especially whether or not he is hypersusceptible. We were all interested, I am sure, when we read in the Journal [40] that the typical histological picture found in the organs in tuberculosis had been produced experimentally by the injection of the waxes from the bodies of tubercle bacilli into several different laboratory animals. The whole of pathology itself seems rapidly to be resolving into just such considerations and possibilities.

The conclusion from the above work, that certain cases of dementia præcox may be of toxic or infectious origin, is almost foregone. With this introduction I wish to present four cases from the records of the Worcester State Hospital, in which the toxic factor was a large one, but was not recognized until autopsy or until certain special tests were applied, namely, the spinal fluid and blood examination by microscopical, chemical and serological analysis.

The first case was that of a female, W. S. H. No. 23119, age fifty-seven, diagnosis dementia præcox. Onset was at forty-four to forty-nine, variously estimated. She was first admitted to the McLean Hospital in 1903. She had been an efficient worker, but gradually came to think that people were talking about her, later expressing the idea that she was boycotted and that people pointed her out on the street. Then she heard the telephone buzzing all night and said that some one kept a lawnmower going another night. She was finally found on the roof, where she went to get rid of the voices. At the hospital her conduct was quiet and natural, but she seemed a little depressed and preferred not to talk about her troubles. She was discharged, but had to return because the scrubgirl made faces at her, as did the priest in church, and voices dictated to her what she should do, and derided her over the telephone. She became exalted and incoherent. She had some insight at first, saying that she could not understand how the voices could be heard, but insisting that

she heard them. Physically her condition was good, and she gained in weight about six pounds. She left the hospital again in 1904 and returned in 1908. She was rather more demented than when she left, but physically she complained only of feeling tired all the time. Her weight dropped steadily from about 160 at last admission to about 90 pounds at death in 1915, a period of seven years. The post-mortem examination showed adhesions in both pleural cavities, with fluid in the left cavity. Both lungs showed masses of tubercles, many of them coalescing and breaking down to form cavities. There were also irregular, circular ulcers in the ileum near the cecum. No discovery was made of the patient's condition clinically, when an X-ray examination of her chest at the outset would doubtless have revealed it.

The second case was that of a male, W. S. H. No. 26963, of unknown age, but thought to be about fifty-two. He was admitted to the hospital in 1910, and died suddenly in 1915 of coronary sclerosis with occlusion and acute hemorrhagic pancreatitis. He had led rather an irregular life, admitted having had private disease twice and having been treated for gonorrhea at Tewksbury. Was told, a long time ago, that he had a chancre. He says he caught the fever at eighteen and his hair came out. He married twice; his second wife was a dissolute woman and was drunk most of the time. She left him about fourteen years ago. Patient admitted arrests and serving sentences and that he drank too much. The onset of his trouble was in 1909, coming gradually and finally terminating in his refusing to pay for a meal at a restaurant one day, on the ground that he owned the place. He was confused and rambling on admission. Said he could hear the voices of his parents and the voice of Jesus. Stated that "when he had his beard on" he could climb a telegraph pole and telephone to any one. He became irritable, silly, demented. After three years he said he could still see God, and later that his father and mother still talked to him, but that he was not bothered any more by it. His physical condition was always good. He took up the work assigned to him and had parole, sweeping up the yards, and so on. He had a scar on the prepuce, a palpable liver and a negative blood Wassermann. The spinal fluid examination was not made. The practice of not taking a Wassermann on the spinal fluid because the blood Wassermann, is negative cannot be too strongly deprecated, as this case with the scar on the prepuce and the abundant history and the next case show.

The third case was that of a male, W. S. H. No. 28853, age twenty-nine on admission, age thirty at death; total duration about two years. The patient was one of 26 pregnancies; 2 miscarried, 18 died in infancy, 1 died of convulsions, 2 boys and 4 girls still living, and one of these has "fits." I cite these facts because there is some question in my mind as to whether the patient was not one of those congenital syphilitics whose disease becomes manifest at a later time than we are in the habit of thinking (Dr. Abner Post, Neurosyphilis Conference, Grafton State Hospital, 1916).

About nine months before admission to the Psychopathic Hospital (No. 2632) the patient had become excessively alcoholic and oversexual. Two months before admission he had auditory hallucinations and thought he was about to be killed. He became maniacal, destructive to furniture and went out at night only partially clothed. He would remain from home a week at a time, contrary to his usual habits. On admission, he said he was "confused in his head." He was inaccurate about his recent movements and about the ordinary facts of his life and of his family. He was easily distracted, and had exalted ideas about his talents as a singer, demonstrating until he was hoarse. Knee jerks were unequal and absent on the left. Admitted to the Worcester State Hospital, he was at first loquacious, showy, euphoric, but became irritable, sullen, resistive, mute and had to be tube-fed. Later he had a convulsion, became wildly excited, then mute, untidy and stuporous. At the last he showed typical katatonic rigidity, with legs drawn up and massive, multiple decubitus developing. At the Psychopathic Hospital the provisional diagnosis had been manic-depressive insanity, manic phase, then dementia præcox, and finally, with the appearance of the Wassermann, general paralysis. The blood was positive. The spinal fluid showed 732 cells, and the globulin and albumin were each 3 plus.

Autopsy showed a scar on the corona, there were dense adhesions in the pleural cavities, and fresh tubercles or gummata were present in the lungs. The pia was thickened and showed whitish plaques. The brain weighed only 935 grams. The frontal poles were pointed, the right being much smaller than the left. The parietal regions were especially soft. The left cerebellar hemisphere was smaller than the right. The posterior columns of the spinal cord were almost confluent.

The fourth case is that of a negress, W. S. H. No. 30094, age nineteen, who was admitted to the Psychopathic Hospital (No.

5918, No. 6412) on March 20, 1916, transferred to the Worcester State Hospital March 29, and died April 2. On March 15 she began to fail, and since she had failed to receive a certain letter from a certain young man, and since she was a mental case, the two facts seemed connected in some hidden manner. But on March 19 she had complained of malaise, anorexia, pain in the epigastrium, and later of a "bursting headache." Her temples beat and her neck felt stiff. That evening, while setting the table, she disappeared, and was not found until the next morning, in an empty room next to her own, where she lay with her throat cut. She slowly recovered from the stupor in which she was found, when she explained that she had been drawing water when her head began to swim and she did not know anything more but that she had felt crazy. Her replies at the hospital were inaudible, given only on close questioning, and she was stupid, apathetic and indifferent. March 26 she developed cerea flexibilitas, muttered through her teeth, and retained her saliva. The breath had a foul odor. She said the doctor told her she was going to have a baby, but admits that she had a menstrual period only the week previously. Pulse was 132, temperature 100-101° F. constantly, respiration 20. She became restless, mute, untidy, resistive, at times shouting and at the end picking at the bedclothes. On March 30 there was a trace of albumin, numerous red blood cells, and numerous hyaline and granular casts in the urine. The sputum was thin, green and purulent, and showed leucocytes and a bacillus morphologically like the influenza bacillus. The post-mortem examination was practically negative, and the case was reported as one of katatonic exhaustion or "Hirntod." But cultures taken from the heart's blood at autopsy showed a bacillus which, in its morphology and cultural characteristics, was the influenza bacillus.

Summarizing, we have two cases of the paranoid form of dementia præcox, both of rather long duration, one male and one female. One died of tuberculosis, the other of hemorrhagic pancreatitis and coronary sclerosis. And we have two cases of the katatonic form, both of comparatively short duration. One died of paresis, the other died of influenza. In one case of the four, only, could the mental diagnosis be questioned. The paretic case could be settled only with the Wassermann technic. The paranoid case with the alcoholic history and the history of chancre might be questioned. All but this one died of an infection. In two of these the infection undoubtedly ran parallel to

the mental symptoms. In the third, which died of tuberculosis, is it too much to imagine that the mental symptoms also paralleled the physical disease?

The microscopic findings were studied by the photographic method on twenty-four sections from each side of the brain in each case. These were arranged according to what we know of the great functional subdivisions of the brain, — the pre-Rolandic and the post-Rolandic, — the latter being divided into parietal, temporal and occipital to correspond to general sensibility, hearing and sight.

The stain used was the Scharlach-R for fat, because it is the most general stain we have for degeneration products of the nervous system, and because it photographs so well.

The sections were cut at 50 micra, with the idea that, if fat were found, it might present itself in some sort of radial or stratified way which would fail to show in thinner sections. This did not prove, in general, to be the case in this series, but the method was carried out, as it appeared logical and gave fair photographs.

In general, the fat was found to be fairly evenly distributed over the cortex, with the exception of that in the alcoholic case. Here it was more marked in the general region of the second to fourth layers, or at least to the layers lying more externally. In the tuberculous case there was a distinct massive process in several regions. In the paretic case the fat was more abundant in the white matter, and this more in the post-Rolandic regions, corresponding to the areas that were noted at autopsy to be the softest. The paretic case was the only one showing any considerable fat in the white matter.

A hint has been given in the above at the topographic idea and at the stratigraphic idea. So far as I have been able to determine, only two writers have attempted any definite correlations between disease of cell layers and dementia præcox, or disease of brain areas and dementia præcox. Cotton,[41] as admitted by Alzheimer,[42] was the first to correlate disease of the second and third cortical layers with dementia præcox, mentioning at the same time that the fat occurs over the entire cortex. Southard [43] was the first to claim a relation between disease of the post-Rolandic areas and dementia præcox of the katatonic form, and between disease of the frontal areas and the paranoid form. Later, Southard and his coworkers have shown some connection between lesions of the angular gyrus and katatonia,[44] gliosis of

the thalamus and dementia præcox,[45] and cerebellar hemiatrophy and katatonia.[18]

Other writers have laid emphasis in their cases on a predominance of the pathological findings in one layer or another, or in one brain area as against another; but no one has made any special claims for these observations before the writers mentioned above. Alzheimer [42] mentioned changes in the deeper layers at first, later pointing out that they occurred in the more superficial layers to a greater extent. Klippel and Lhermitte [46] found the changes more in the zones of association, in the large pyramids of the third layer of cells and in the fusiform cells of the sixth layer of Hammarberg. Dunton,[46] in a case of katatonic dementia præcox dying of pneumonia, found chromatolysis most marked in the fifth layer of Hammarberg. Lubouchine [47] mentions the molecular layer and the layer of the small pyramids; Lannois and Paviot [48] mention the Purkinje cells of the cerebellum; Koller [49] mentions increase of glia in the superficial layers and in the white matter; Elmiger [50] mentions the free edge as being most affected; Orton [51] finds the ameboid changes more in the deeper layers and in the white matter; Sioli [52] finds more change in the upper layers; Mott [53] in the infragranule layers. As for the fibers, Cramer [1] mentions thinning of the interradiary and tangential systems; Weber,[32] the supraradiary network; Eisath-Hall,[54] Meynert's layers. All have support in the shape of corroborative work by other investigators.

Dunton [46] and Maschtschenko [55] claim that the frontal lobes are more affected; Zalplachita,[56] the frontal and central; Orton,[51] that the temporal and occipital are less affected than other parts; but no one has, so far as I can learn, investigated the question of topographical distribution in and for itself, except the writer mentioned above.

The four cases here presented can add little of a decisive nature to these great questions. Only one case presents anything of interest to the stratigraphic question. That is the case of the paranoid with the alcoholic history, who died of hemorrhagic pancreatitis, and his history and physical examination make the diagnosis of dementia præcox somewhat doubtful. However, in his case we do not have to consider the effects of an intercurrent or of a causative infection upon the cell picture, as we do in the three other cases. In his case the fatty changes were more in the outer layers. Topographically, his case was rather indefinite, the fat occurring mostly in the areas of audition

and of general sensibility. The fact that the fatty degeneration is rather marked in the temporal regions in this case is especially interesting in view of the continued auditory hallucinations which the patient experienced, but the fact of its absence in other areas may mean either that the cells in those areas are exhausted, or that they were not affected, at least at the time of the patient's death. To determine whether they were really exhausted would be an especially interesting research in view of ideas entertained that there is a relation between frontal lobe lesions and paranoid dementia præcox.

The idea that the power of the nerve cells to produce fat has been exhausted in those areas where the fat is not found is given support by the findings in the second case of paranoid form, dying of tuberculosis. This case was especially chronic, lasted longer than the first case, and clinically showed much more profound deterioration. From our knowledge of the occurrence of fat in the various pathological processes, we should expect to find an abundance of it here, and yet we find much less than in the first case. The idea gains credence that the fat-producing power is exhausted. In this case there were large masses of fat present, reaching macroscopic size in places, and doubtless connected with the tuberculous processes in the lungs and the intestines, but in general the whole cortex appeared exhausted.

The case of the young katatonic who died of influenza has a most interesting distribution of the fat in the small elements of the cortex, especially in the glia cells and the blood vessel walls. The blood vessels are especially prominent, also, even the finest capillaries standing wide. The fat is distributed here in all layers and in all areas. It is in the most labile elements, the elements which are the most easily affected according to all writers, and the disease process was so fulminating that the nerve cells themselves have scarcely had time to react. Perhaps this case, together with the two previous ones, may give us some idea as to the fat-producing period of the nerve cell. It is evident that no topographic or stratigraphic ideas could be drawn from this case.

The last case, that of the paretic with katatonic mental picture, is striking by reason of the enormous amount of fat to be seen, and because the fat is confined for the most part to the white matter. The question arises here, as in the cases above, whether the cortex is involved at all, or whether it is exhausted. Perhaps we have a type of paresis involving the fibers more

especially and the gray matter rather less, just as it has been suggested (Southard [57]) that there are two types of feeble-mindedness, — the type with plenty of pathways, but little to go over them, and the type with plenty of receivers and senders, but few wires. The topographical significance in this case is great because the chief degeneration was found in the post-Rolandic regions, corresponding to the katatonic picture presented by the patient; and at autopsy, the especial softness of the parietal areas was noted.

With such an array of pathology as presented in the literature and in the histories and examinations of these patients, one should hesitate to make an unqualified diagnosis of dementia præcox, in the manner in which such diagnoses are made in many hospitals. There are few uncomplicated cases of dementia præcox. The question of a faulty diagnosis, the placing of a patient in the class of dementing psychoses of unknown cause, is often a difficult one to settle, but the attempt should always be made, and methods should be added to the diagnostic facilities of most of our hospitals for the insane. Even in this small number of cases the paretic one would most certainly have been missed had the patient's blood proved negative to the Wassermann examination, and if it had been examined from certain of our hospitals. I have repeatedly taken the spinal fluid post mortem, where the examination was refused during the life of the patient on the ground that the blood was negative, and I have repeatedly found it positive to the Wassermann, chemical and microscopical examination. In the case of the katatonic, the true picture would never have been revealed had it not been for the extensive bacteriological examination post mortem. Morphology is not enough to identify an organism. Extensive culturing, before and after death, and a microscopic examination of the tissues at autopsy, with the well-known stains for bacteria, will often yield results in many cases of our so-called dementia præcox. Do not forget to stain for the tubercle bacillus. And soon we will come to a splitting of the dementia præcox group, here in America, into a lot of little groups, each on its own etiological basis. The beginning has already been made in splitting off those with a positive Wassermann reaction and other positive tests on the spinal fluid. Who knows how many are caused by influenza or tuberculosis or alcohol?

Beyond this talk of the individual case stands the interest in the group, and for most of us this interest crystallizes into the

demand for the *why* of the mental picture. Like the why in any question concerned with the human body, we must go for the solution to physiology before we can understand abnormal functionings. The brain is divided into several great regions according to this point of view, and hence our necessary interest in topography. On the mental side, in recent years, great efforts have been made to get at the roots of the ideas entertained by psychopathic subjects. Such efforts have rapidly departed from the teachings of the original founders, and have drifted into a miserable, nondescript state which I have been tempted to call "neo-mysticism." Such a state was far from the minds of the founders, I am sure, for they said, in speaking of hysteria,[59] that the mechanisms which they had discovered could develop only on a constitution predisposed. And I take it that some of our ultra-moderns, even, are coming around that way, for I note that some account for their lack of success with the method by saying that the patient "did not have the 'stuff' in him," meaning by that, I suppose, that the patient was defective from the start. What makes the whole thing so mystical is not that its advocates deny the operation of physical elements, but that they behave as if they did. It is of little moment for one to admit that there is a constitution behind the patient's trouble, if in the next moment he tries to right the patient's difficulty by letting loose some pent-up ideas from the subconscious personality of the individual, such ideas always to be sexual in nature. This I take to be the gist of the difference between "neo-mysticism" on the one hand, and Freudianism of the true sort with its psychoanalytic method on the other. Some writers and workers have come to recognize this difference, and so we see the attempt being made to resolve character into other elements than the sexual alone, and I think a truer picture will be presented — though we run the risk of being suspected of having certain complexes ourselves, you know, by trying thus to avoid the issue.

But what has come out of all this is a method, and the method can be of value to the anatomist. If this method can resolve the faulty character into its elements, and these elements can be correlated with the abnormal functioning of known physiological regions, we have an extremely valuable method indeed. Something of this sort might be expected from the introspective method of experimental psychology. By introspection, under experimental conditions, it is possible to resolve complex feelings, emotions and ideas into simpler elements which are visual, audi-

tory, kinesthetic, etc., but we can never get patients to introspect under experimental conditions. Is not the psychoanalytic method the one to be used in resolving the patient's experiences into elements? Something may also be expected to come from the study of the behavior in the sense used by the experimental psychologist whose special field is the behavioristic side of physiology. But the study of the behavior of an insane individual is aided by the explanations of that individual, if those explanations can be analyzed, and how can they be analyzed at the present time except by the psychoanalytic method? Let us take, for example, the sign so often seen in dementia præcox, confusions of all sorts, and in the deliria, — the removing of the clothing. The patient is said to be denudative. The reasons for the removal of the clothes under improper conditions may be various. One may say it is a sign of exhibitionism; another that the clothes irritate the patient because the skin is hypersensitive; and so on almost *ad libitum*. But we may gain something if we ask the patient about it. He may give a valuable answer directly, or we may arrive at a valuable conclusion as to the reason by piecing his replies together, as the psychoanalytic method does.

À propos of asking the patient questions, I am reminded of a striking incident which was observed during an intraventricular treatment for paresis. The patient became restless just as the needle was passing through the cerebral substance. Asked what the matter was, the patient replied that he would be all right if the doctor would stop "making his mouth [patient's] fill up with spit," and that his mouth was actually filling up with saliva was not imagination. Beside giving the reason for his restlessness, his reply gave a cue to a second very important point, — that a cerebral injury may affect a gland-secretion. Ceni [59] has also shown changes in the cells of the testicles of roosters by subjecting them to cerebral injury.

The suggestion to use the psychoanalytic method along truly Freudian lines and not in the hazy way in which it is now being applied by his successors, for the most part, should be made now. But the application of the psychoanalytic method in this new way will have to wait until those using it recognize that there is something more beneath character than sex, and that there is something more in personality than character alone. I mean by this that personality includes much more in its connotation than the word character includes. And only when these two are

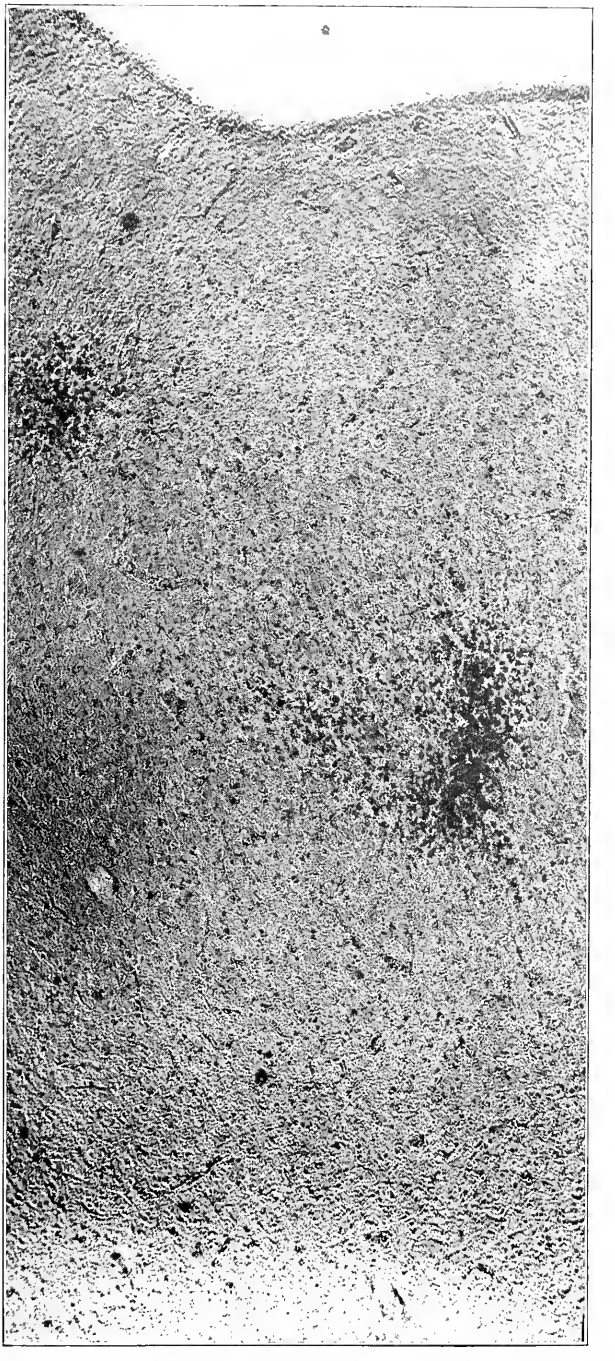
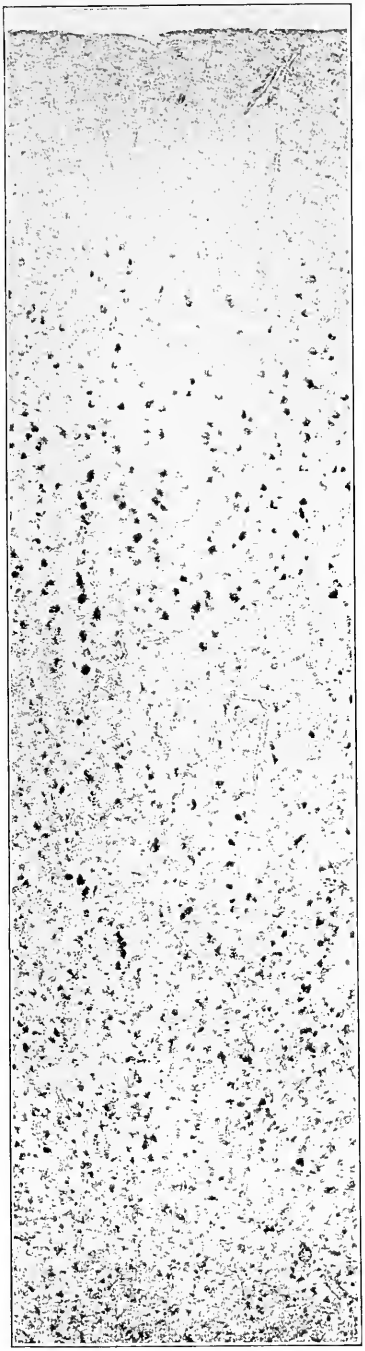


FIG. 1. — Case 1, tubercular paranoid dementia præcox. Cortex of the right superior occipital gyrus, showing two massive processes probably related to the patient's tuberculosis. Section cut 50 micra. Scharlach-R stain. Photograph takes in cortex to white matter.



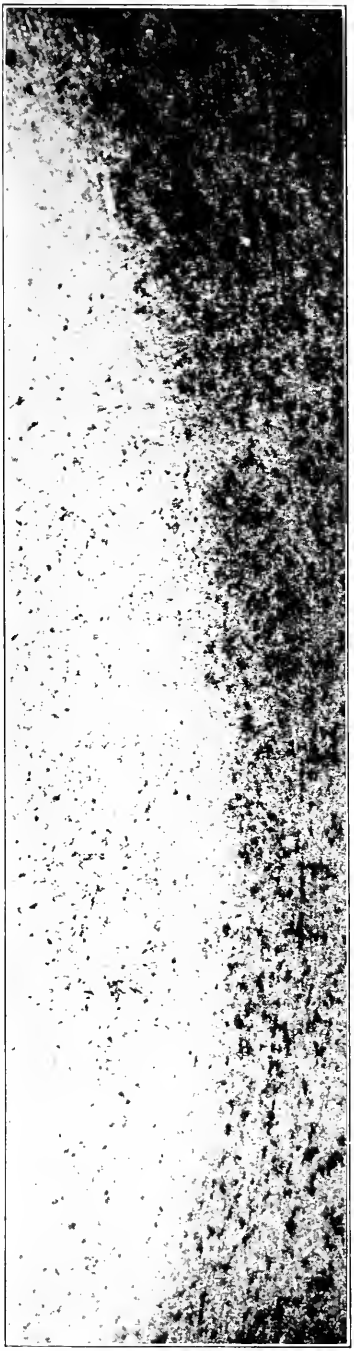


Fig. 2.

Fig. 3.

Fig. 2. — Case 2, alcoholic paranoid dementia præcox. Cortex of the left supramarginal gyrus, showing the fat to be chiefly in the outer layers of the cortex. Section cut, stained and photographed as in the previous case.

Fig. 3. — Case 3, paretic-like katatonic dementia præcox. Cortex and white matter of the left lingual gyrus, showing the large amount of fat in the white matter and the small amount in the cortex, with the sharp line of demarcation between the two which appeared in many sections. Staining and cutting same as before, but photograph includes only the white and the cortex at the bottom of a sulcus.

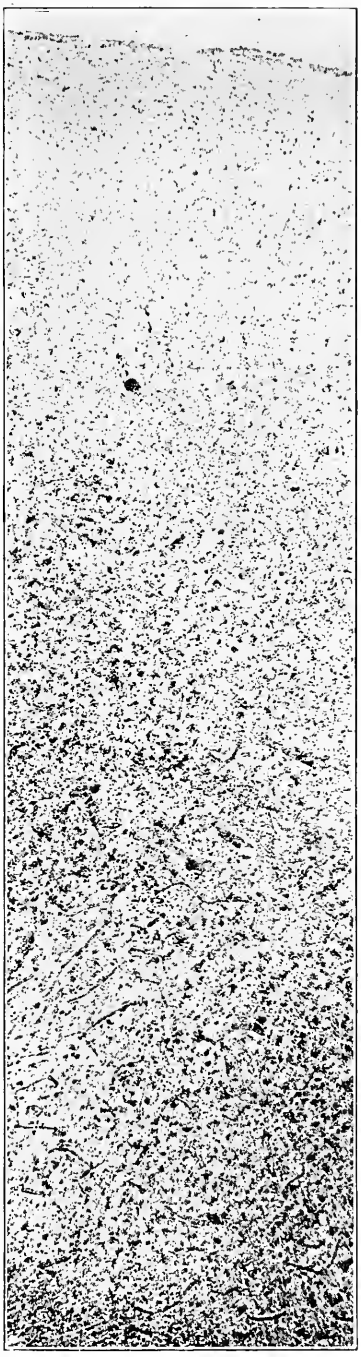


FIG. 4. — Case 4, influenza katatonic dementia præcox. Cortex of the right quadrate gyrus, showing the distribution of the fat in the small elements of the entire cortex, fairly evenly distributed. Staining, etc., as in Cases 1 and 2.

recognized will the psychoanalytic method be of value for the topographical study of the cortex lesions of the insane, and for the correlation of those topographically distributed lesions with the mental picture presented by the patient.

The requisites for future advance, then, are the recognition of unrecognized work, — recognition of the fact that the central nervous system of dementia præcox patients gives evidence of abnormal life processes in the cells; that the same changes are present in the intoxications and the infections, in the confusions and the deliria; that there are methods at hand for diagnosis which are not being used; and that the diagnosis is often difficult and often wrong and will often be wrong when we have exhausted all our methods, but an intelligent attack will have been made.

Conclusions.

1. That cases of dementia præcox, of confusional insanity or of delirium, of pseudotumor, and of various other mental conditions have pathological changes which are similar.

2. That it is quite *à propos* to assume that certain cases of dementia præcox are due to infectious or toxic processes, in proof of which four cases are introduced, one of which is definitely syphilitic, one is alcoholic and possibly syphilitic, one is tubercular, and one is a case of influenza of fulminating type.

3. That cases which can be detected are being missed because of the lack of application of diagnostic methods. As an example, the refusal to permit a spinal puncture where the blood Wassermann is negative is especially decried.

4. That topographic studies are next in order as offering a logical direction of research in solving the why of the mental picture, later to be followed by stratigraphic studies.

5. The idea is suggested that the psychoanalytic method may reduce the mental condition to elements which can be correlated with lesions topographically or stratigraphically disposed.

In conclusion, I wish to express my thanks to those who have shown their interest in this work, of whom there are many, and also to my laboratory assistant, Julius H. Stean, who assisted materially in making the sections and the photomicrographs.

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A CASE PRESENTING AN EPIDERMOID PAPILLARY CYSTOMA INVOLVING THE THIRD VENTRICLE.*

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General Neuropathology of the Case.

Epidermoid growths involving the third ventricle have created particular interest with reference to their relation to the pituitary body and the disturbance of its function, the possibility of localization of such tumors, and their source of origin.

Recalling the epiblastic origin of the neural tube, one is not surprised to find, in close relation to the central nervous system, ectodermic cells originally intended for skin and mucous membrane. They may develop as if they were in their normal location with the formation of dermoid cysts or cholesteatomas.

The presence of epidermoid tissue in the third ventricle may be explained as being the result of an infundibular anlage. Cushing [1] reports two examples of infundibular cysts filled with a yellowish gelatinous substance, and with numerous verrucose nodules composed of squamous epithelium projecting from the walls, which he considers as possible developmental aberrations in relation to the neurohypophysis. Similar infundibular cysts were described by Langer [2] and Strada.[3]

Saxer [4] reported a tumor which he believed originated from the epithelial lining of the ventricle, or the pars intermedia of the pituitary body, the gland being normal.

Mott [5] mentions the possibility of epidermoid tissue being transported by the vessels which grew into the third ventricle to form the choroid plexus, also of its having arisen from cells of the hypophyseal diverticulum.

The hypophysis or anterior lobe of the pituitary body originates as a pharyngeal diverticulum (Fig. 1). The exact location of its origin with reference to the juncture of the pharyngeal and buccal epithelium is still a matter of dispute. Minot [6] considered the diverticulum an outgrowth from the ectodermal lining of the mouth. Normally, the cells forming the original stalk atrophy

* From the Massachusetts State Psychiatric Institute, Massachusetts Commission on Mental Diseases. This paper was one of a series presented to Dr. E. E. Southard on the occasion of the tenth anniversary of the establishment of the Bullard Professorship of Neuropathology, Harvard Medical School, 1906 to 1916.

and the hypophysis loses all connection with the epithelium of the oral cavity. It is not uncommon, however, to have a retention of some cells along the stalk tract, and Erdheim [7] in cross sections of normal glands found inclusions of pavement or ciliated cells near the superior and inferior portions of the hypophyseal cleft and within the gland, presumably representing "rests" of the primitive ectodermic diverticulum. He recorded seven heteroplastic tumors probably arising from such "rests."

Dean Lewis [8] emphasizes the frequency and importance of tumors arising from craniopharyngeal duct epithelium; reviews the literature with special attention to cases reported by Wagner, Langer and Harbitz, and describes a case. He presents a table by Creutzfeldt, published in 1908, showing that in 55 necropsies

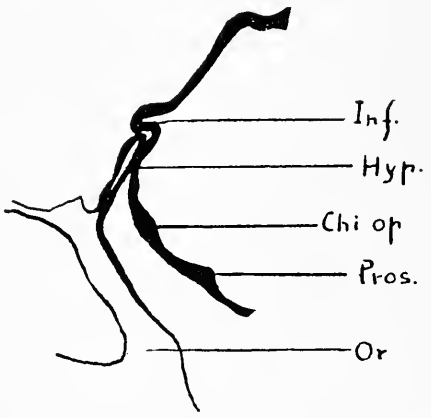


FIG. 1. — Origin of the hypophysis as a pharyngeal diverticulum: Inf., infundibulum; Hyp., hypophysis; Chi. op., optic chiasm; Pros., prosencephalon; Or., mouth.

of tumors of the hypophysis without acromegaly, 19 were classed as craniopharyngeal duct tumors.

In the 30 cases of tumor of the third ventricle reported by Weisenburg,[9] only 3 are stated to be epidermoid in character. These include the cases of Saxer and Mott.

In the case here presented the growth did not show the large polygonal cells with densely staining protoplasm, characteristic of tumors of the pars intermedia, nor did it resemble those arising from the choroid plexus. The infundibulum was distended, and its tissue partially replaced by the tumor with a suggestion of a tumor stalk near the right ventrolateral surface. Cross sections through the third ventricle and pituitary body, which was removed intact still attached to the brain, showed the dura-like

capsule of the growth to be continuous with the connective tissue of the gland. The pituitary gland was normal. The squamous epithelium of the tumor showed a suggestion of intercellular spines and well-marked scaling; but no hair or sebaceous material was found. Vacuolization and cilia formation are not differential, and there does not seem to be any adequate criterion by which one may judge how this epidermal tissue happened to be in this location. From the situation and character of the growth it probably originated either as a result of a developmental abnormality of the infundibulum or from an hypophyseal "rest."

In the grouping of third ventricle tumors according to symptomatology, suggested by Weisenburg [9] in an excellent review of thirty cases of which he reports three, this case would be in Class 1; *i.e.*, those cases in which a tumor of moderate size is situated in the floor of the third ventricle, and in which there is no extension into the foramen of Monro or the aqueduct of Sylvius. Though the aqueduct was not dilated, the posterior part of the ventricle and the peri-aqueductal structures were apparently involved indirectly, as shown by the pupillary disturbance, without, however, paralysis of associated ocular movements and a reeling gait suggestive of involvement of the red nuclei or superior cerebellar peduncles.

The patient's tendency to drag his feet and the weakness of the legs might be interpreted either as evidence of pressure on the internal capsules or of cortical injury.

One of the early symptoms in this case was the evidence of hypopituitarism (loss of sexual power, transient polydipsia and polyuria, and possible gain in weight). These may have been due to the fact that, occupying the base of the third ventricle, the growth at an early date interfered with the discharge of a secretion of the posterior lobe of the pituitary gland directly into the cerebrospinal fluid, or to disturbance of function due to pressure on the whole gland. Histologically, no change was noted.

Another striking feature was the drowsy, somnolent, apathetic condition of over a year's duration, with periods approaching normality. Weisenburg does not consider this feature as specific of lesions of the third ventricle, but due to impairment of the normal function of the cortex, the result of pressure against the skull through dilatation of the lateral ventricles. Mott also believed it to be the result of compression of the cortex by

internal hydrocephalus, and explained the recurrences by the escape of fluid from the lateral ventricles, thereby relieving the cerebral compression and removing the cerebral anemia. Purves Stewart [10] considered that somnolence in these cases was associated either with direct upward pressure on the third ventricle or with secondary anemia from compression of the vessels at the base of the brain. Turner [11] thought that it was due to cerebral edema. Cushing [12] notes hypersomnia in many cases of hypopituitarism, and suggests, though certain cases showed sufficient increase in cerebral tension to possibly account for the drowsiness, that the condition may be associated with changes in glandular function. This relation has been considered as an explanation of normal sleep. The case reported by Purves Stewart, in which a sarcoma (extracerebral) destroyed the pituitary gland without clinical evidence of somnolence, is in opposition to this theory.

In the case under consideration there was an internal hydrocephalus with increased intracranial pressure, cerebral anemia, edema and pituitary disturbance; it was not a suitable case for determining whether somnolence is a general diffuse effect, or results from the involvement of a focal center, possibly in the floor of the third ventricle or pituitary body.

The mental condition (change in disposition, enfeeblement of memory, disorientation, untidiness, etc.) is compatible with the fact that the chief gross evidences of pressure were in the prefrontal areas. Sections from the second and third frontal gyri on the left showed loss of myelin in the fibers of the zonal layer. There was a slight diminution in the number of cortical cells, and those present showed considerable chromatolysis.

Areas involved by Tumor. — The tumor directly involved by pressure the gray substance and fiber tracts about the third ventricle, including: —

(*a*) The anterior commissure containing fibers between the two hippocampal regions (pars temporalis), and those derived from the lobus olfactorius connecting the olfactory tract on the one side with the hippocampal region on the opposite side (pars olfactoria).

(*b*) The fornix composed of fibers arising in the hippocampal region, pursuing an arched course to the corpora mammillaria. Some fibers terminate here, others cross the midline and turn downward into the reticular formation as far as the pons.

(*c*) The lamina cinerea and lamina terminalis, a thin layer of gray substance between the corpus callosum and chiasma, con-

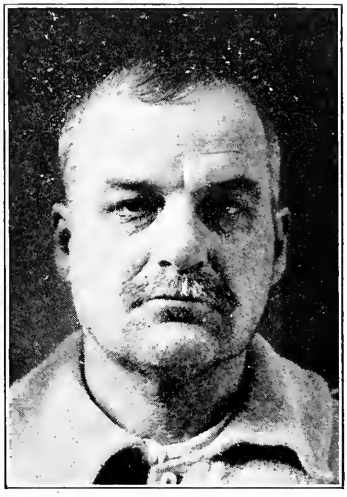


Fig. 2. — Patient, May 10, 1914.

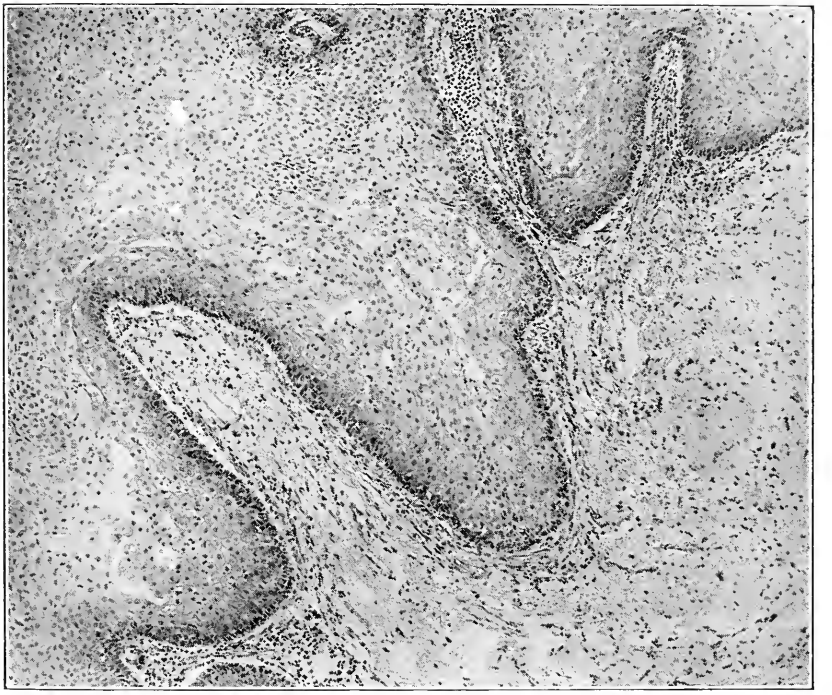


FIG. 3. — Papillomatous character of the growth, type of epithelium and connective tissue stroma. Hematoxylin and eosin, × 70.

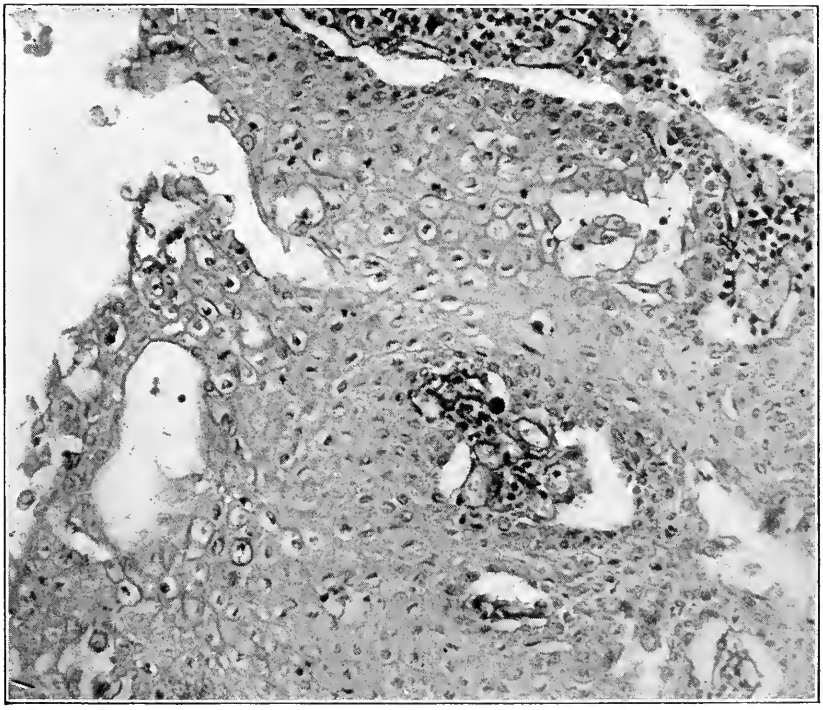


Fig. 4. — Inner aspect of cyst cavity. Hematoxylin and eosin, × 215.

FIG. 5. — Relation of the tumor to the thalamus. Cellular infiltration of the connective tissue. Hematoxylin and eosin, × 225.

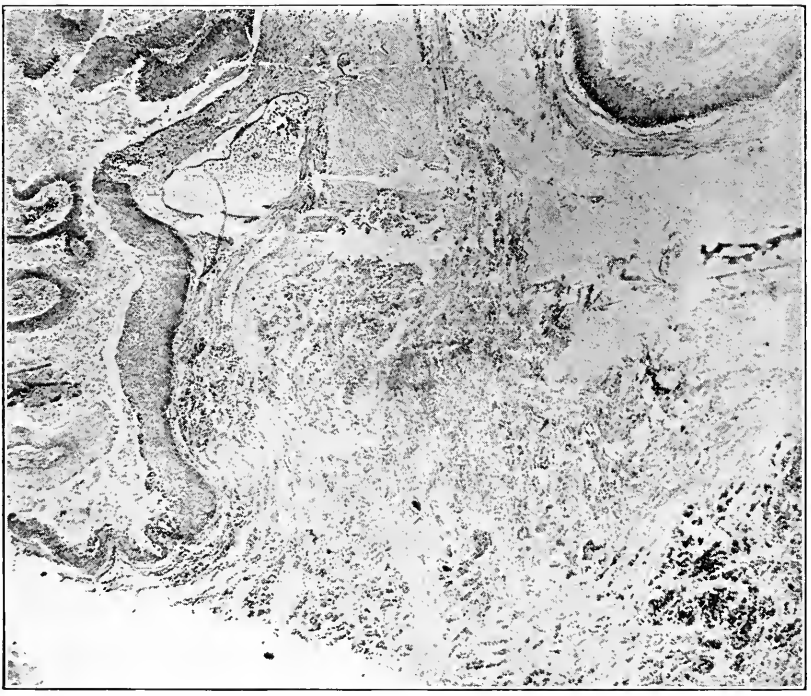


FIG. 6. — Relation of base of growth to the pituitary gland. Globule of hyalin material. Hematoxylin and eosin, × 23.

tinuous above the chiasm with the tuber cinereum and connected at the side with the gray substance of the anterior perforated space.

(*d*) The optic chiasm and the optic tract, especially on the left, were distorted and flattened. The disks showed a marked papilledema and deposition of new tissue.

(*e*) The tuber cinereum — a lamina of gray substance extending forward from the corpora mammillaria to the optic commis-

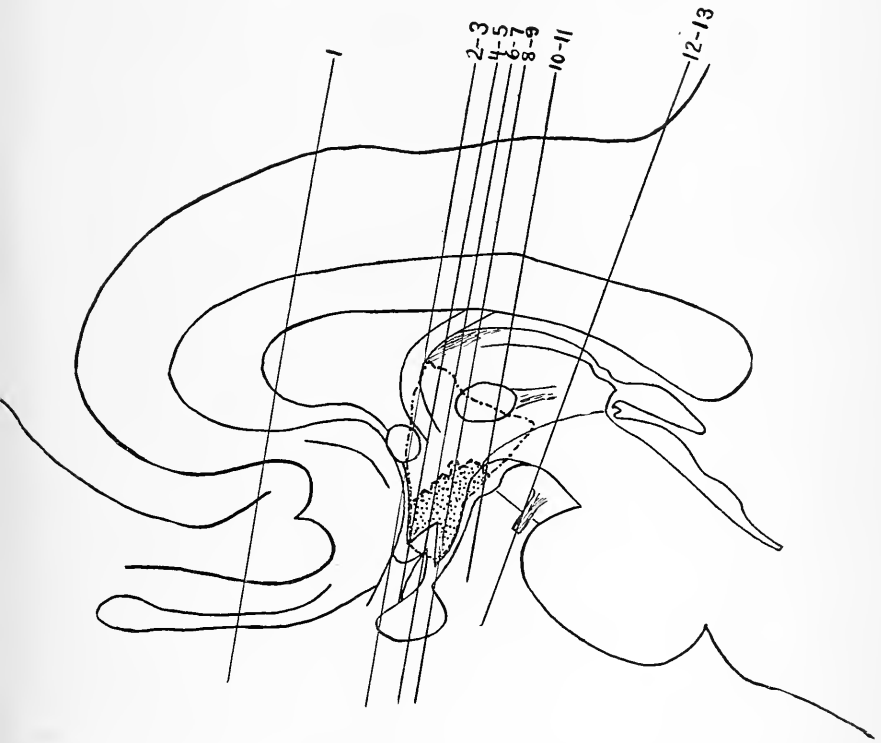


Plate C. — Diagram of medial sagittal section, showing outline of the cyst and levels at which the following frontal sections were made: —
In plates 3, 5, 7, 9, 11 and 13 one is looking toward the posterior pole of the brain.
In plates 2, 4, 6, 8, 10 and 12 one is looking toward the anterior pole of the brain.

sure to which it is attached. It presents several small collections of ganglionic cells; the lateral eminences; the eminentia vascularis, homologue of the saccus vasculosus of lower vertebrates, especially prominent in the fishes. Johnston [13] considers the eminentia vascularis as possibly an organ for controlling the character of the spinal fluid. The basal optic ganglion (supra-optic nucleus Cajal), — a tract of gray matter with nerve cells,

lying to the outer side of the tuber cinereum close to the optic tract. From each a tract issues, which, after decussating with that of the opposite side (Meynert's commissure), applies itself to the mesial side of the optic tract and passes back to the lenticular nucleus (Déjerine).

(*f*) The corpora mammillaria, especially the mesial nuclei. Efferent tracts: Bundle of Vicq d'Azyr to the dorsal or anterior nucleus of the thalamus; bundle of Gudden to the red nucleus and adjacent gray matter of the tegmentum.

Afferent tracts:[14] (*a*) by way of the columns of the fornix, and (*b*) through its peduncle from the main fillet and arcuate fibers in the tegmentum.

(*g*) Posterior thalamic decussation,[15] behind the mammillary bodies, probably a connection between the corpora Luysii (Déjerine).

(*h*) The intermediate gray mass or middle commissure, uniting the mesial nuclei of the thalamus across the third ventricle and continuous below on each side with the gray matter of the cavity.

(*i*) The mesial series of nuclei of the thalamus (Cajal). There was no suggestion of a thalamic syndrome in this case.

(*j*) Hypothalamus,[16] — the prolongation of the tegmentum under the posterior part of the thalamus, divided by Forel into three layers from above down, — the stratum dorsale, zona incerta and the corpus subthalamicum or nucleus of Luys, the latter having taken the place of the substantia nigra lying next to the prolongation of the crusta.

(*k*) The internal capsule. The possibility of determining capsular involvement was complicated by the cortical injury.

It has been difficult to estimate the degree of injury suffered by the tissues adjoining the growth, and even more difficult to correlate the injury with any clinical manifestations because of the diffuse area involved and the paucity of data as to the normal physiologic function of the structures.

Clinical Details.

The case was under the direction of Dr. Frankwood E. Williams.

History. — The history of the patient, a man, aged 52, white, was obtained from his wife. The family history was not important. He had been subject to headaches and vomiting in early life. At 33 he had typhoid fever. His application for life insurance had been rejected six years before because of albuminuria. He had pertussis in 1913. He

denied venereal disease. He had lost sexual power one and one-half years before. He used no alcohol, and no drugs, but smoked a cigar occasionally.

The patient had been well until August, 1913, when he had occasional severe frontal headaches and complained of not feeling well. During the following months he had frequent headaches accompanied by constant nausea, but not by vomiting; he was abnormally sleepy and extremely irritable. In February, 1914, he drank large quantities of water, sometimes eighteen glasses in an hour; he again became lethargic and confused mentally, but was not considered seriously ill. He gave up his work. In April he was frequently disoriented for time, his memory was poor, and his vision seemed to be failing. His speech became thick; he began to drag his feet, and he developed incontinence of urine.

He was admitted to the Psychopathic Department of Boston State Hospital, May 7, 1914. At first he was excited, tore his blankets and sheets into strips and tied them in a fantastic manner about his feet. He was oriented for person, but not for place or time. There was a marked loss of memory for both recent and remote events with a tendency to fill the gaps with fabrications. He had some delusions of grandeur, magnifying the amount of his wealth and assuring the staff that he built all the buildings around the hospital. Definite evidence of hallucinations was not obtained. Emotionally, he ordinarily had been self-reliant, very cheerful, even-tempered, social (got on well with people), reserved but never seclusive. At the time of examination he appeared self-satisfied, somewhat euphoric and inclined to be restless. He had no insight into his condition.

Examination. — Physical: The patient was a well-developed and well-nourished man, 5 feet 8 inches in height, weighing 203 pounds, stripped. His face was flushed. The general examination was negative except for very slight edema over the feet and shins. The systolic blood pressure was 150 mm. of mercury.

Neurologic: The pupils were central, the right slightly larger than the left, and both were irregular. Consensual reaction and reaction to direct light were sluggish. Accommodation was normal. Extra-ocular movements were normal. There was no ptosis, strabismus or nystagmus. Examination was made of the fundi by Dr. Gerhardt in consultation, May 25, 1914. There was slight hyperemia of the disks, not pathologic. The deep reflexes were normal. Abdominal and cremasteric reflexes were not obtained. The gait and station were normal. There were no areas of anesthesia or hyperesthesia. There was no tenderness over the nerve trunks. Muscle sense was retained except for slight inaccuracy in the finger-to-nose test.

Laboratory Studies. — Urine: An occasional slight trace of albumin and a rare hyalin cast were found in the urine. A study of the acidity by the hydrogen-ion concentration method[17] gave evidence of a slight acidosis (plus 0.9, two hours after 4 gm. of bicarbonate of soda). The phthalein output was 18 per cent. The time was not stated.

Blood: The Wassermann reaction was negative. The cytologic examination was negative. Quantitative examination of uric acid, urea and non-protein nitrogen showed a nitrogen retention (100 per cent increase over the maximum normal values as given by Folin and Denis [18]).

Spinal Fluid: Three examinations were made. Cells, 2 to 6. Globulin was negative, and albumin was found in small amounts. The Wassermann reaction was negative. The colloidal gold test was negative for syphilis. There was 100 per cent total non-protein nitrogen increase. Urea at the pathologic threshold, based on normal values given by Mestrezat. [19]

Head: Roentgenographic examination of the head was negative June 24, 1914.

Course of the Disease. — During the spring and summer the patient remained confused, retarded and apathetic, took no care of his person, was untidy, and was frequently found lying about exposed. In October, because of the slight acidosis shown by the laboratory studies, he was given sodium bicarbonate by mouth. He became oriented for time, place and person; his memory improved, and he appeared to take more interest in current events. There were still periods when he was confused and when he had some difficulty in locomotion. At times he would walk like a drunken man. He had lost 39 pounds. Though not well, he was allowed to go home. In three weeks he returned in a confused state, continually incontinent and very untidy. He remained in bed and refused to eat unless fed. There were a few short periods when he would brighten up and seem to know what was going on about him.

Jan. 3, 1915, after a febrile period of three days (white count 16,800), he became stuporous and died.

Summary. — The patient was a man of 52 years, who had been ill for sixteen months, and whose past history was negative except for typhoid fever nineteen years before and pertussis one year before the present history. There were loss of sexual power; rather acute onset of severe frontal headaches, with nausea but no vomiting; irritability and drowsiness, with increasing mental confusion; transient polydipsia; speech defect; difficult equilibration; disturbance of vision; disorientation; memory defect with tendency to fabrication; expansive delusions; restlessness; untidiness, with a lack of appreciation and indifference to his condition.

Physical Signs: The right pupil was larger than the left. Both were irregular and reacted sluggishly to light. There was a slight speech defect. There were tremor of the extended fingers, increasing weakness of the legs, a tendency to drag the feet, and a loss of control of both the rectal and vesical sphincters.

Laboratory Findings: All tests for syphilis were negative. A slight trace of albumin and casts was found in the urine. There was low kidney function. The blood pressure was 150 systolic. There was retention of

nitrogenous products in the blood and spinal fluid, and an increased white count shortly before death.

The case was presented at a meeting of the staff of the Psychopathic Department May 16, 1914. It created considerable interest and discussion; but no censensus of opinion was reached. It was noted that the case clinically resembled general paralysis; but such diagnosis would hardly be ventured with all tests for syphilis negative. The picture in some respects simulated the terminal stage of Korsakoff's syndrome, but presented no etiologic factor, as alcohol or other toxic agent. No definite indication or localizing sign of arteriosclerosis was present. The evidence of chronic infection, pyogenic or tubercular, was not convincing. Brain tumor was considered; but there were negative eyegrounds, and no localizing signs; an intracranial growth was considered improbable. Although the findings were not typical of uremia, because of the low kidney function, retention of nitrogenous products in the blood and spinal fluid and urinary findings, the case was classified as a cardiorenal psychosis.

Necropsy. — Two hours after death, necropsy was performed by Drs. Solomon, Bunker and Bloomer.

A summary of the positive findings with reference to the body is noted in the anatomic diagnosis.

Kidneys: They weighed 240 gm. They measured 11 by 5 by 2.5 cm. Five small cysts dotted the surface. The capsules were slightly adherent and the pyramids were poorly differentiated.

Thyroid: It was firm, and section showed nothing of note.

Suprarenals: They were very small, the cortex measured 0.1 by 0.2 cm. in thickness. Two lines of the cortex approximated in one limb; the second limb was separated by a brownish medulla which showed a slight hyalin change in one suprarenal.

Pancreas: It was normal.

Testes: Threaded well.

Head: Description of the brain is given by Dr. Canavan. The hair was somewhat scant. The periosteum was negative. Calvarium measurements were: frontal, 1 cm.; temporal, 0.4 cm.; and occipital 0.7 cm. Depressions for the pacchionian bodies were slightly to the right of the median line and pierced the inner table at the vertex. Grooving for the middle meningeals was shallow on both sides.

The dura was not adherent, but was tense; and the brain filled the dura completely. Convolutions were seen through the dura. There was no subdural fluid; and on peeling back the dura mater, the pia appeared not to be present, only a tracing of irregularly injected vessels pressed on a smooth brain surface. The pial surface of the brain was dry.

The superior surface of the brain tended to assume a round form when placed on a flat surface. The hemispheres strained from each other. At the frontal poles, particularly on the left, the convolutions were smooth and pressed out in appearance. The sulci were indicated on the right.

The swelling of the brain and the widening and flattening of the gyri were most marked anterior to the posterior lobules. Even the mesial surface showed the flattening of convolutions, especially on the left in the prefrontal region.

At the base of the brain the vessels were small, the vertebral arteries were unequal, the left being larger than the right. There was some hyalin change in the middle cerebrals, but no sclerosis. The middle cerebral artery on the left appeared very small, and its lumen tiny.

The olfactory bulbs were red and slightly unequal; but the tracts were white. There was a sharp differentiation between the bulbs and the tracts.

The optic chiasm was flattened from pressure beneath, especially on the left side, and the form of the optic nerves was much distorted. The optic chiasm measured a little more than 2 cm. from side to side, and spread for a distance of nearly 1 cm. on the left. The tract which leaves the chiasm for the geniculate bodies on the left was broad and thin in appearance from pressure of a swelling from beneath. The distal ends of the optic nerves appeared infringed on and did not assume their round contour, but were irregularly wishbone in shape. The space between the chiasm and the mammillary bodies was translucent gray, it measured 3 by 3 cm., and a puncture of it for securing fluid from the third ventricle showed a thick, purulent, pinkish semifluid substance, a smear from which by Gram's stain, showed many large mononuclear cells with large nuclei; some polymorphonuclears that looked remarkably small in comparison. There were no organisms. When stained by Wright's stain they showed polymorphonuclears (small), red blood cells, and large endothelial and transition lymphocytes. The lobus pyriformis on either side was flattened and thin. The pons measured 4 by 3 cm. and the medulla 2 by 2 cm. The third nerves were involved in a thickening of the pia which forms a part of the floor of the third ventricle.

The optic nerves in their orbital portion showed nothing of note.

The middle ears, Gasserian ganglions and pituitary gland were negative.

The brain's weight was 1,575 gm. Tigges' formula 8 by 172: 1,376 gm. The gain in brain weight was 199 gm.

The cord was firm and showed nothing of note.

A frontal section revealed a marked difference in size in the anterior section of the lateral ventricles, the right measuring 4 by 3.5 cm. at the wider end, and 1.5 cm. at the inferior portion. The left ventricle cut at the same plane measured 5.3 by 4.2 cm. at the upper, and 1.5 cm. at the inferior. On cross section of the third ventricle, the tissues were found to be soft and edematous, and the capacity of the third ventricle markedly increased.

Anatomic Diagnosis. — The man was well nourished. There were: injection of appendix; sclerosis of the coronaries and aorta; chronic fibrous endocarditis, tricuspid; chronic fibrous endocarditis, mitral; chronic fibrous endocarditis, aortic; fenestration of the aortic valve; apex

— scar; pulmonary congestion; chronic interstitial nephritis; chronic perihepatitis; a cyst in the liver. The calvarium was thick; the pia dry; the brain was swollen and smooth. Chronic internal hydrocephalus. Chronic cerebral abscess of the third ventricle and hyaline basal vessels were present. The brain weighed 1,576 gm., the gain in brain weight being 199 gm.

Microscopic Findings. — The visceral organs were fixed in Zenker's solution, embedded in paraffin and stained by eosin and methylene blue and Mallory's connective tissue stain.

Kidneys: There was focal infiltration of the interstitial tissue of the cortex by cells of the lymphocytic series. There was a rare sclerosed glomerulus, compatible with a slight degree of chronic vascular nephritis. They were essentially normal kidneys for a man of 52.

Pituitary: There was normal glandular structure.

Testes: The spermatogenous epithelium showed development of spermatocytes and occasional spermatids, but no mature spermatozoa. There was a decrease in the interstitial cells.

Thyroid, suprarenal and pancreas showed no pathologic change.

Spleen: The capsule was thickened. A large amount of intracellular dark brown pigment was present. There was an increase in the connective tissue of the end arteries. Malpighian bodies showed some edema and focal destruction of cells with amyloid deposits.

Liver: Formaldehyd fixation followed by sudan III showed increase of fat in small droplets, chiefly around the portal vessels.

Other organs showed increase in connective tissue around vessel walls. There were a large number of eosinophiles in the lymphoid tissue of the large intestine.

The brain and other nervous tissues were fixed in liquor formaldehyd embedded in celloidin, and stained by the methods of Weigert and Marchi, and with cresyl-violet for cell studies.

Longitudinal sections through the heads of the optic nerves showed the disks to be twice the normal thickness, with retention of a definite cupping but deposition of new tissue. There was slight cellular infiltration along the more minute vessels. The retina showed low folds near the disks. There were distention of the vessels within the optic nerves and marked dilatation of the intervaginal spaces with the arachnoid prominent. Cross section of the left nerve showed a small triangular area with loss of myelin.

Peripheral Nerves: They were negative.

Sympathetic Ganglions: The nuclei were centrally placed. There was peripheral arrangement of the Nissl substance and abundant pigment.

Gasserian Ganglion: The cells were large, and the nuclei were centrally placed. The Nissl substance was finely granular, and evenly distributed through the cells. Few cells showed pigment. The cells were shrunken from the nucleated sheaths.

Cord: Sections from the cervical, thoracic and lumbar regions showed

no loss of myelin. A few of the anterior horn cells at each level were filled with fat in very fine droplets.

Sections of the tumor were stained with cresyl-violet, hematoxylin and eosin, Mallory's phosphotungstic acid hematoxylin, Verhoeff's elastica and Van Gieson.

The cyst appears encapsulated by a supporting layer of vascular connective tissue on which is a stratified epithelium, varying in thickness from a few to many cells with extensive desquamation of the superficial layers. There is a tendency to the formation of prickle cells, but no epithelial fibrils or "pearls." Mitotic figures are not numerous. Though the contour of the infundibulum is essentially retained, its tissue is largely distorted by the growth which fills the cavity and which, in this region, appears as a papillary cauliflower-like mass. On the right ventrolateral aspect there is more abundant vascular connective tissue with radiations into the papillæ suggesting a tumor stalk. There are several finger-like projections and a small cystic protrusion latterly from this area. In the center of the basal proliferation there are a few narrow spaces surrounded by a single layer of large deeply staining columnar vacuolated cells resembling goblet cells, and occasionally a few columnar cells with a suggestion of cilia formation. No hair or sebaceous material was found. The stroma is relatively small in amount, contains numerous blood vessels and in some places is infiltrated with polymorphonuclear leukocytes. There are a number of finger-like projections from the tumor, but no definite break in the connective tissue capsule was found. The capsule resembles dura in structure, and is continuous with the connective tissue about the pituitary gland which was removed intact with the brain. There are a few hyalin globules just below the growth between it and the gland.

There is some gliosis of the surrounding brain tissue, and there is evidence of retrograde metamorphoses. There are numerous collections of polymorphonuclears and endothelial cells containing fat and pigment. Some areas seem to have undergone a hyalin degeneration.

There are none of the large polygonal cells with densely staining protoplasm characteristic of tumors originating from the cells of the pars intermedia. The growth has not the extensive vascularity or angiomatous character frequently seen with plexus tumors.

Sections from the second and third left frontal convolutions were stained with Weigert, Marchi and cresyl-violet. There is a loss of myelin in the fibers of the zonal layer as compared with Campbell's charts. The cortical cells are slightly decreased in number. The remaining cells appear edematous. Frequent cells show eccentric, poorly staining nuclei and diminution in the Nissl substance. This is more marked in the larger cells. Marchi preparations show an increased fat content in a few of the ganglion cells. There is no phagocytosis.

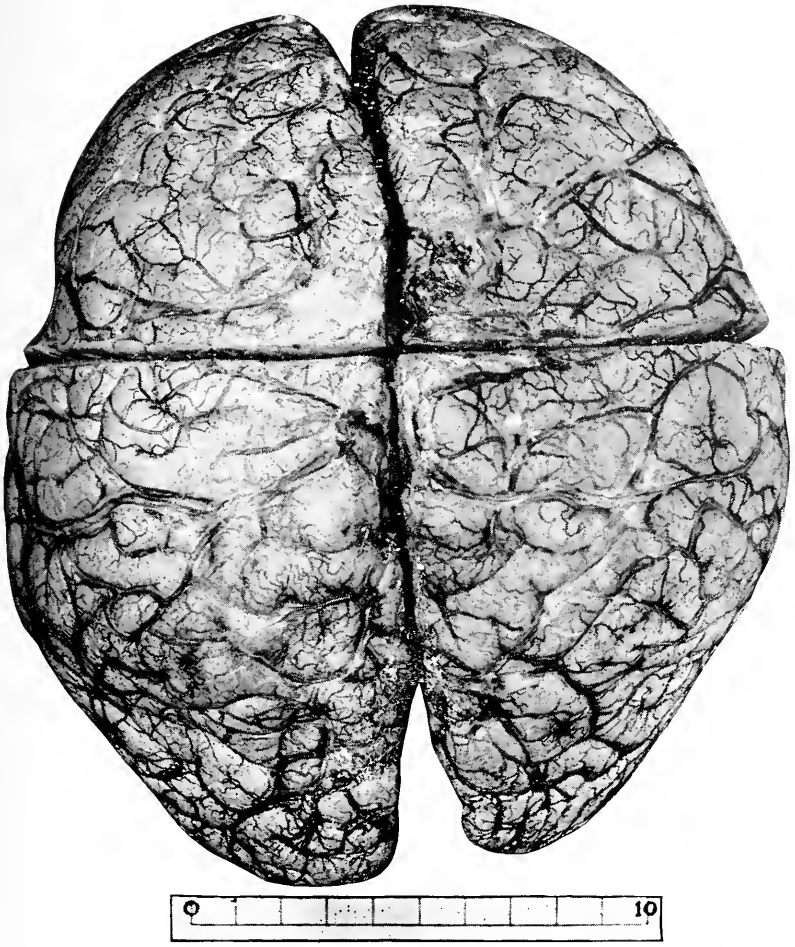


PLATE A. — Upper surface of the brain. The brain before fixation tended to assume a round form when placed on a flat surface. The brain surface was dry, with a tracing of irregularly injected vessels. The convolutions were pressed out in appearance, the sulci being indicated on the right. The swelling of the brain and the widening and flattening of the gyri were most marked anterior to the posterior parietal lobules. The mesial surface also showed the flattening of the convolutions, especially on the left in the prefrontal region.

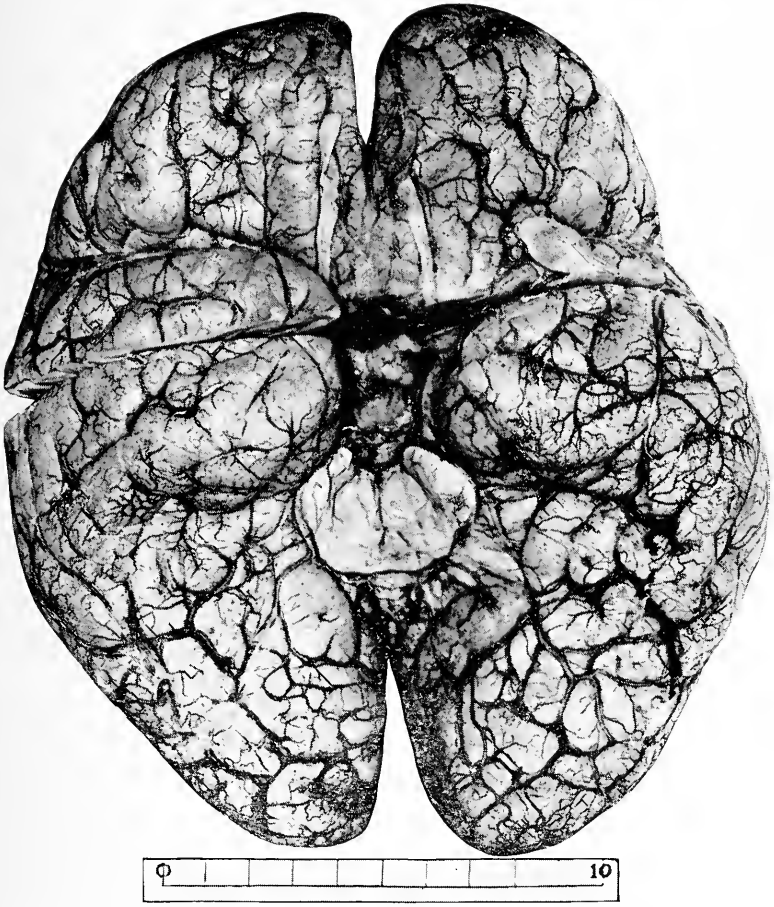


PLATE B. — Lower surface of the brain. The vessels were small with inequality of the vertebrals. The left middle cerebral appeared small, and its lumen tiny. There was some hyalin change in the middle cerebral vessels, but no sclerosis. The olfactory bulbs were red and slightly unequal. The optic chiasm measured 2 by 1 cm.; it was much distorted as though from pressure beneath. The optic tract on the left was broad and bulging, the right less so. The optic nerves were flattened. The tuber cinereum was translucent gray. There was a small nodular protrusion of tissue on the right. The pituitary was normal in size and consistence. There were several grayish yellow spots on the surface. The mammillary bodies were slightly flattened.

The pituitary gland, removed attached to the brain, appeared normal in size and outline.

The mammillary body on the left appeared swollen as though from pressure from beneath.

The third nerves were involved in a thickening of the pia between the peduncles. The brain stem in sections at the level of the red nuclei which appear as circular areas just dorsal to the substantia nigra and crusta.

The cerebellum appeared normal.

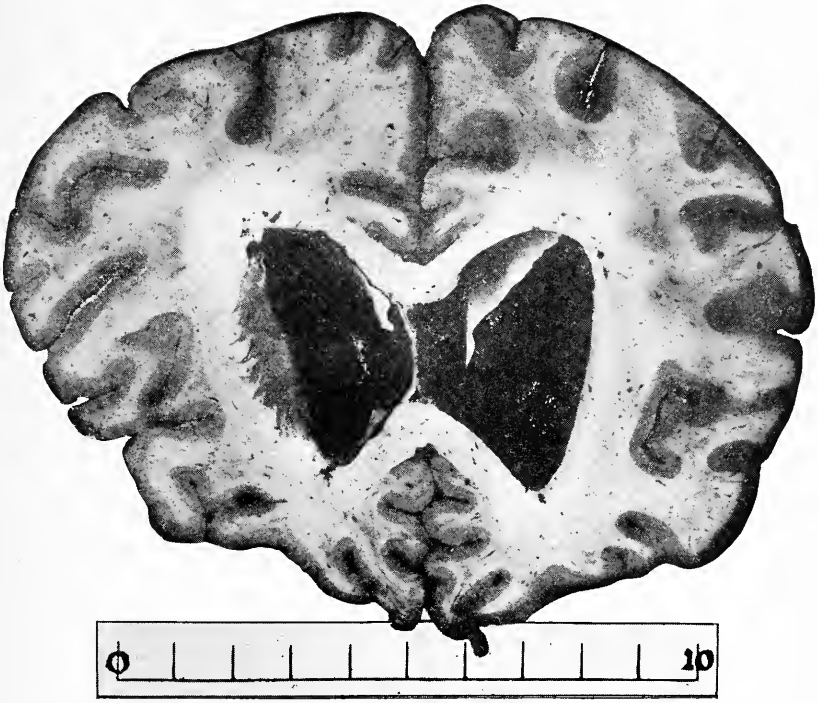
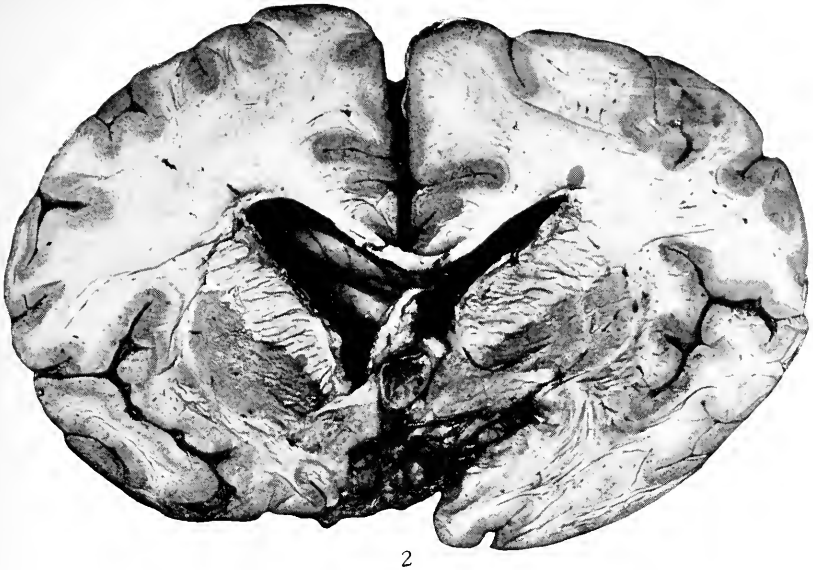


PLATE 1. — Frontal section just posterior to the genu corporis callosis. Slightly oblique. The septum pellucidum extends between the truncus and rostrum corporis callosi. Lateral to the anterior horns of the ventricles is the stratum subependymale, and on the right the corpus striatum before its division into the nucleus caudatus and the nucleus lenticularis by the traversing fiber bundles of the internal capsule. Converging toward the corpus striatum are seen the strands of the corona radiata. The olfactory bulb and tract are folded back beneath the section. The increased size of the left ventricle may be noted.



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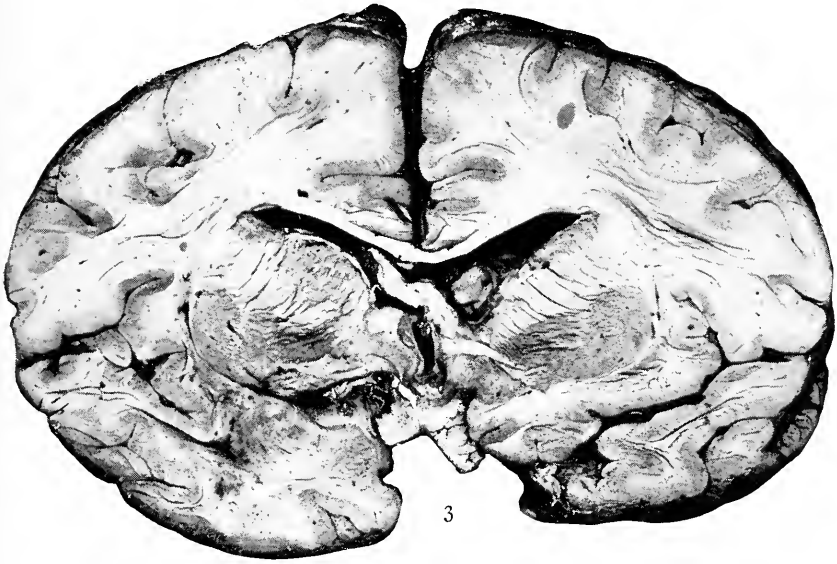

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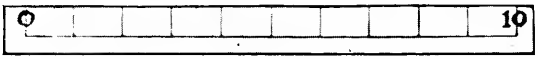
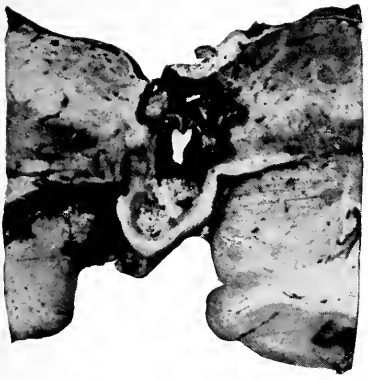


PLATES 2 and 3. — Oblique section. Left side shows more anterior level than the right. The internal capsule appears dividing the corpus striatum into the now small caudate, and the lenticular nuclei. The latter shows a subdivision into the globus pallidus and the putamen. On the right ventral to the corpus striatum lies the substantia perforata anterior, on the left the tuberculum olfactorium. The fibers of the anterior commissure are seen crossing the ventral part of the globus pallidus on the left, more laterally on the right. Ventral to the septum pellucidum appear the fiber bundles of the fornix, more prominent on the left.

Posterior to the recessus triangularis, rather loosely held to, but distorting, the columnæ fornicis, anterior commissure and lamina terminalis is seen the sacular termination of the cyst occupying the base of the third ventricle. The foramen of Monroe is seen on the left. The increased size of both lateral ventricles may be noted.



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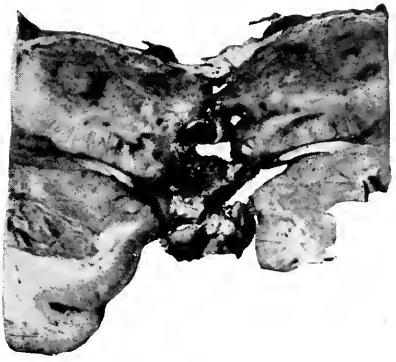

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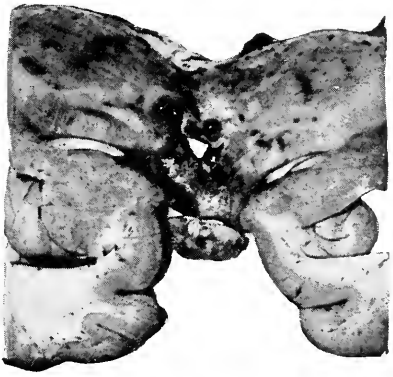

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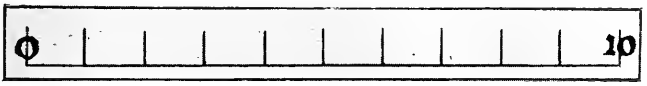
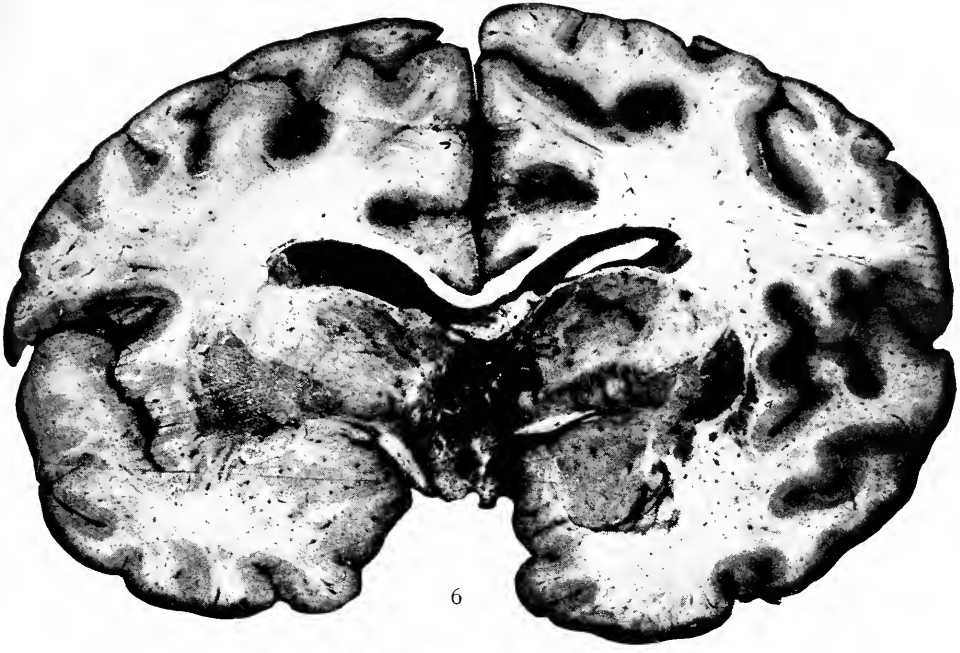


PLATES 4 and 5. — On the left the section strikes through the anterior end of the thalamus. The columnæ fornicis lie lower on both sides, while the cruræ assume a dorsal position. Their attachment to the corpus callosum has been torn. On the right, the thalamus exhibits differentiation into the nucleus anterior, and the nucleus lateralis and the nucleus amygdalæ appear within the temporal lobe. The third ventricle is increased in size, irregular in outline and almost completely replaced by the cyst. There is a free upper surface which lies folded on itself across the distended upper portion of the ventricle. The grayish limiting wall can be traced in apposition with the remaining structures about the ventricle. The basal portion of the cyst contains a whitish cauliflower-like growth displacing the fibers of the optic chiasm, more markedly on the left, and causing the rounded swelling of the left optic tract noted in the description of the base of the brain. Around that portion of the growth, extending into the pocket in the optic tract, is a semicircular mass of colloid material.

PLATES 8 and 9. — Section passes through the anterior end of the massa intermedia which is flattened by the distention of the third ventricle and pressure of the cyst which protrudes into it from below involving chiefly the mesial nucleus of the thalamus and bundle of Vicq d'Azyr on the right. There is a small pocket between the cyst wall and the overlying commissure on the left. The portion of the third ventricle above the massa intermedia is flattened but patent. The infundibulum is filled with the growth which bulges into the left side. The pituitary in section shows grayish areas. Microscopic preparations were made from this section.



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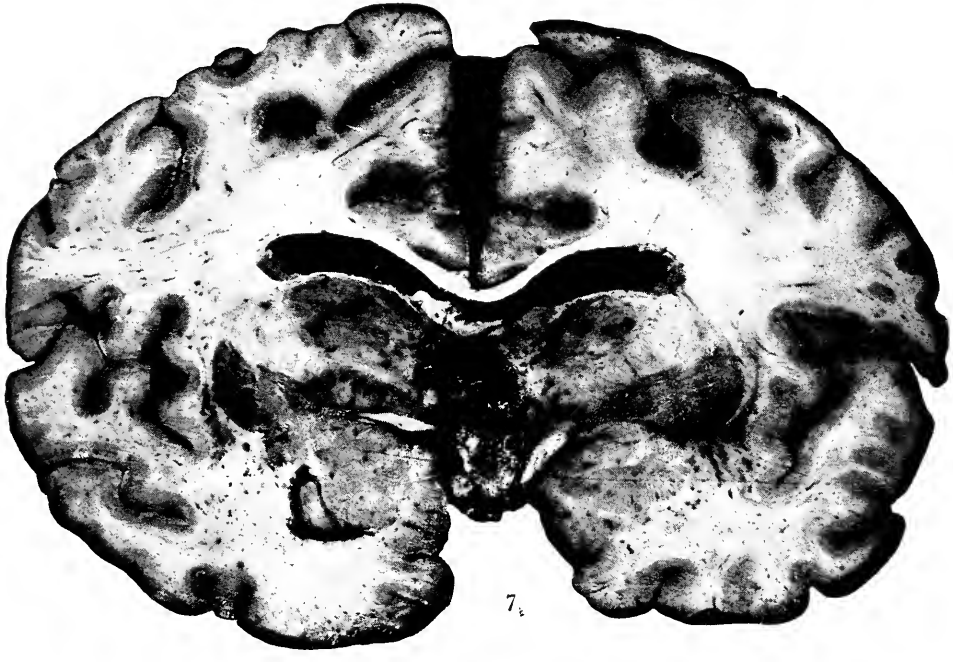

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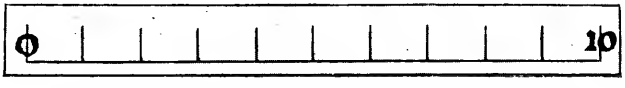
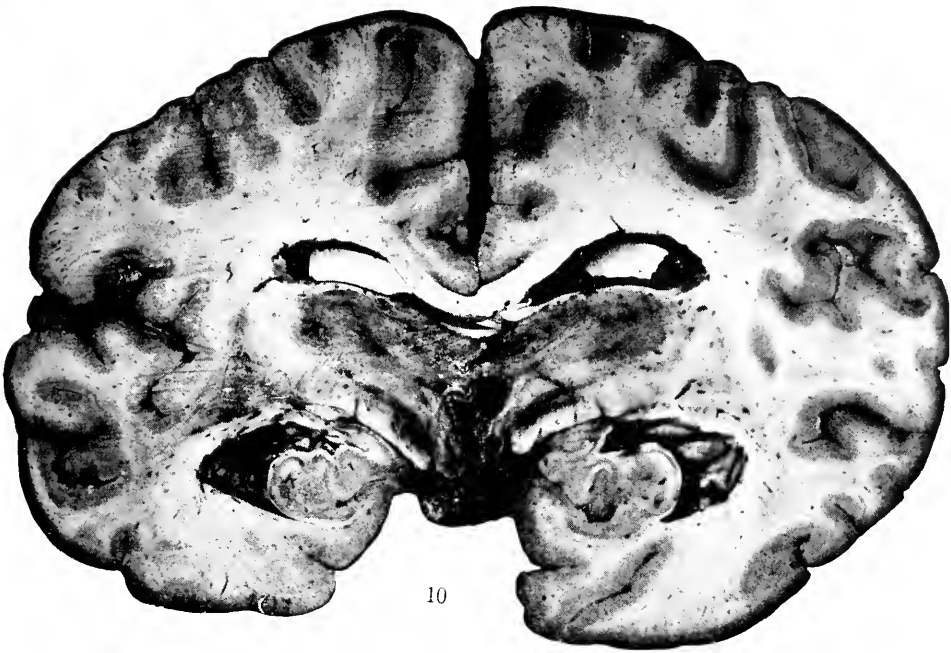


PLATES 6 and 7. — The distention of the third ventricle is more marked; the tumor mass at the base of the cyst now filling the tuber cinereum is larger, and there is a small knob-like extension of the growth on the right. There is marked distortion of the optic tracts. The columnæ fornicis lie deeper. The relation to the thalami, and, on the right, approximation to the internal capsule which now penetrates farther baseward and is traversed ventrally by the fiber strands from the nucleus lenticularis assembling to form the fasciculus lenticularis (Forel) may be noted. Microscopic preparations were made from the anterior portion of this section.



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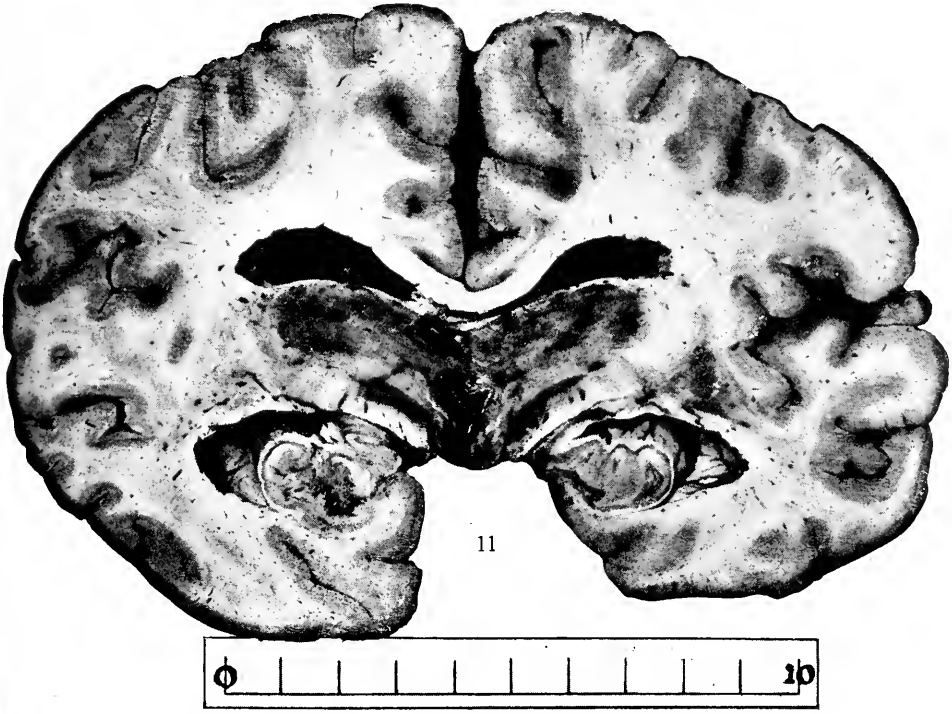

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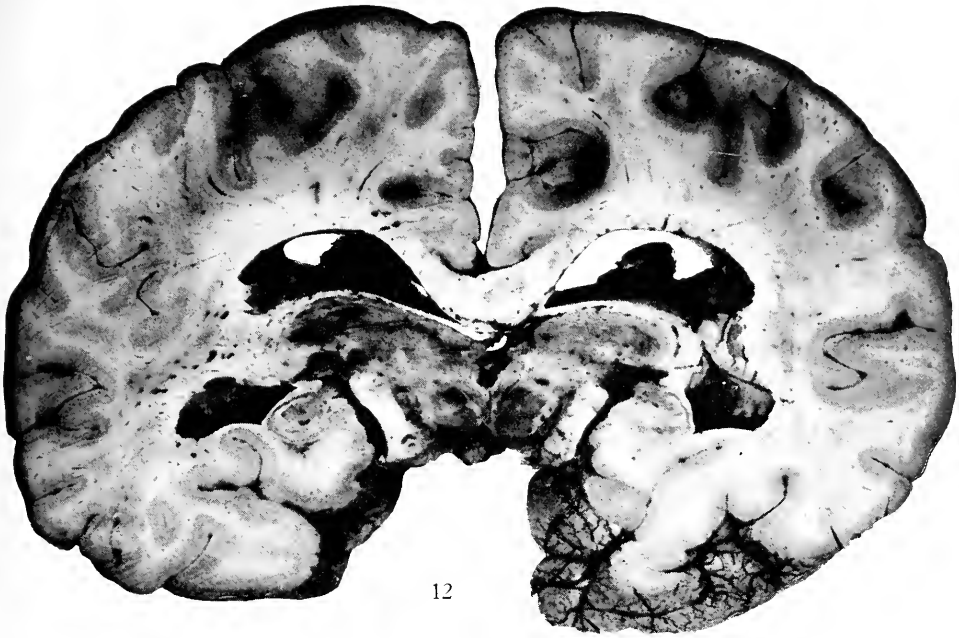
PLATES 10 and 11. — Section passes obliquely through the posterior portion of the massa intermedia and the mammillary bodies. Separating the latter and completely occupying the lower portion of the third ventricle, the cyst is triangular in shape, and there is no growth in the basal portion at this level. The terminal fibers of the fornix are seen entering the lateral nucleus of the mammillary body, and the bundle of Vicq d'Azyr ascending from the mesial nucleus toward the anterior nucleus of the thalamus. Weigert's specimen from the anterior portion of this section shows no loss of myelin in the surrounding structures.



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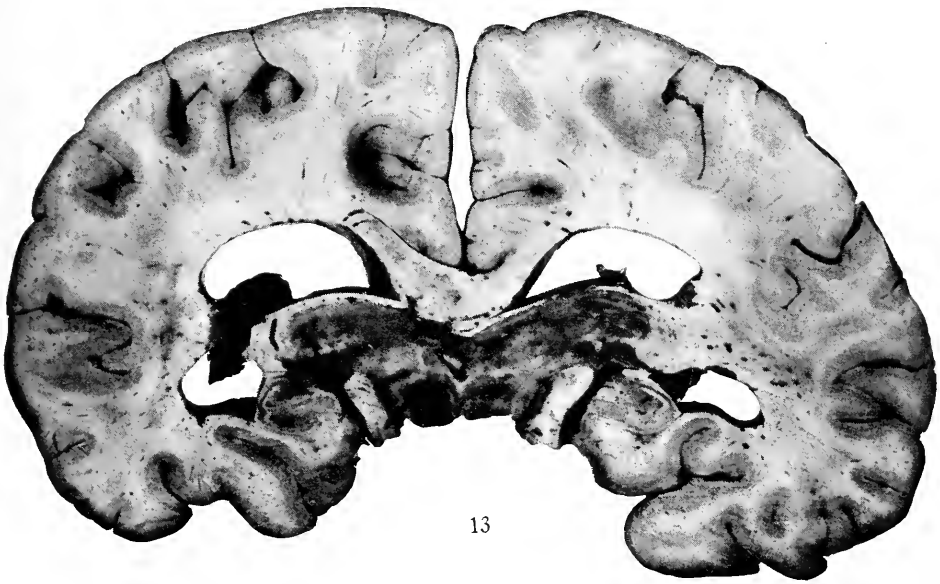

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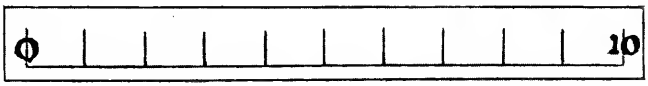

PLATES 12 and 13. — Oblique section behind the massa intermedia and passing through the red nuclei. The posterior portion of the cyst wall is seen in the third ventricle lying below the massa intermedia just anterior to the red nuclei. There is dilatation and flattening of the third ventricle above the massa intermedia. Sections at this level stained by Weigert and Weigert-Pal show no lesion.

Summary.

In this case, presenting an epidermoid papillary cystoma involving third ventricle, the tumor probably originated either from a hypophyseal "rest," or as a result of a developmental abnormality of the infundibulum. The clinical signs and symptoms of sixteen months' duration did not lead to a localization before death. Correlation of clinical and pathologic findings has been complicated by the difficulty of separating local from remote and general effects, and the paucity of data as to the normal physiologic function of the structures involved.

It gives me great pleasure to acknowledge my indebtedness to Dr. E. E. Southard for creating the atmosphere that made this study possible, and for constant stimulating and helpful suggestions.

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ABSENCE OF LOBUS OLFACTORIUS AND SCLEROSIS OF CORNU AMMONIS.*

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Cases showing absence of the olfactory lobe are rare. In 1914 Weidenreich [1] reported one case and quoted nine others from the literature on this subject. Kundrat,[2] in his monograph, "Rhinencephalie," describes brains which have no olfactory lobe, but are combined with other brain anomalies. Besides these two reports I was able to find one case reported by Valenti.[3] But according to Weidenreich all reports which he quoted lack detailed information, especially in that they do not discuss the area of the brain supposedly connected with the olfactory nerve and therefore called "rhinencephalon." Valenti's report contains no statement about this area.

In Weidenreich's Case there was entire absence of the bulbus and tractus olfactorius in both hemispheres. We assume that the rhinencephalon governs the sense of smell as found by Broca and Zuckerkandl in their studies in comparative anatomy, and by Retzius embryologically. If this is true also in man, we should be able to see some change in the parts regarded as the olfactory center in brains that have no olfactory lobe. Weidenreich investigated carefully his case that dealt with the bilateral absence of the bulbus and tractus olfactorius, absence (right) and reduction (left) of the tuber olfactorius. Except for these defects, no parts of the brain regarded as the rhinencephalon showed any marked change which denotes atrophy; but he was not able to study his case histologically because of the unsuitable previous treatment of the material for this purpose. He concludes the question of the olfactory center with the sentence: "Auch die Lösung diesser Frage bleibt also aufgespart, bis der Zufall eine neue Beobachtung des Defectes bringt und zugleich die Möglichkeit einer sofortigen Untersuchung am frischen und entsprechenden fixirten Material."

It is many years since Broca and Zuckerkandl announced that the gyrus fornicatus must be regarded as the cortical olfactory area (it must be understood that under the name gyrus fornicatus

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or rhinencephalon are included gyrus cinguli and gyrus hippocampi with cornu ammonis). Although I am inclined to believe that certain portions of the rhinencephalon govern the smell sense, the part that subserves this function is still unknown, especially in man.

The authors quoted are arranged according to the year of publication.

Examination of animals has convinced Ferrier (cited in Bechterew's paper) that the olfactory center is located at the lower extremity of the temporal lobe. Munk (also cited by Bechterew) seeks it in the neighborhood of the cornu ammonis.

Onodi [4] concludes, after investigation of the hitherto published clinicopathologic reports concerning the sense of smell, that the olfactory center might be traced into the gyrus hippocampi and the uncus.

Ramón y Cajal,[5] from a histological study of the brains of several animals as well as that of man, has reached the conclusion that the focus spheno-occipitalis, the subiculum, the focus praesubicularis and the cornu ammonis seem to have no direct connection with the olfactory nerve fibers, and that they probably represent the tertiary olfactory center.

Campbell,[6] chiefly from histologic study of the human brain, recognizes the cross relation between the lobus pyriformis (frontal pear-shaped part of the gyrus hippocampi) and the cornu ammonis, but he doubts whether Ramón y Cajal is right in regarding the latter as a tertiary olfactory center. One of his conclusions is, "Histology supports comparative anatomy in suggesting that in the human brain the lobus pyriformis must be regarded as the principal cortical center, although not the sole one governing the olfactory sense."

Brodmann [7] distinguishes the gyrus hippocampi from the surrounding areas on the ground of the histologic construction, and names it "area ento-rhininalis."

Bechterew [8] concludes, from the results of experimental investigation on sixteen dogs, that an olfactory center is located apparently in the lobus pyriformis, and that this must be regarded as the perception center for the sense of smell, while perhaps the neighboring region (subiculum cornu ammonis, Bechterew) may have the function of its conception.

Edinger [9] seems to approve the cornu ammonis for this center chiefly from the comparative anatomic standpoint.

As I have mentioned above, our knowledge of the olfactory

center is limited. Campbell declared, after covering the histologic evidence: —

> Above all things we seem to lack the knowledge which in the case of some other cortical regions has proved so valuable. I refer to that derived from studies in pathological history; for instance, we have much to learn of the cortical changes attending uncomplicated atrophy or lesion of the olfactory bulb and peduncle, and have virtually no conception as to what subdivisions such changes would be distributed over.

Fortunately, through the generosity of Dr. Southard, I was permitted to investigate a brain that had no olfactory tracts. I will give the macroscopic and microscopic findings of this rare and interesting case, describing particularly those parts of the brain which have been suggested as having intimate connection with the olfactory sense. I shall endeavor to throw some light on the question of the olfactory center which seems to be so obscure.

Report of a Case.

History. — F. S. H. 228, S. B..I. 1916. 87 (from the record of the Foxborough [Mass.] State Hospital), R. R., a man, aged 45, had epileptic dementia, the probable cause of which was heredity. The psychosis had been of gradual onset and of over fourteen years' duration, and had been characterized by periodic attacks of an epileptiform nature during which the patient lost consciousness, had generalized clonic convulsive movements, bit his lips and tongue and had loss of sphincter control. Following these attacks the patient was weak, befogged and depressed. He also had periods of depression and at times of excitement, auditory and visual hallucinations, with delusions of persecution. His judgment and emotional fields were markedly impaired, and there was general mental deterioration with no insight. He was admitted to the hospital April 17, 1907, and died July 13, 1916. Necropsy was performed by Dr. M. M. Canavan eleven hours after death.

Anatomic Diagnosis. — This included brown atrophy of the heart muscle; ascites; calcified lymph node in mesentery; bladder distended; chronic perisplenitis; sclerosis of the mammary arteries; hydrothorax; hydropericardium; sclerosis coronaris; tricuspid and mitral stenosis; chronic fibrous endocarditis, mitral; chronic fibrous endocarditis, aortic; acute vegetative endocarditis, aortic; possible bronchopneumonia; pulmonary infarcts; accessory spleen; uric acid deposits, kidney (?); pigmentation, fibrotic spots; focal opacities, pia; absence of lobus olfactorius; soft cerebellum.

Macroscopic Study of the Brain.

In general form and size the brain was about normal. The pia mater showed focal opacities in the frontal and motor regions, and was non-adherent. The gyri in general were of normal richness and appearance and almost symmetrical. On the base of the brain the absence of the bulbus and tractus olfactorius first attracted our attention (Fig. 7). There was slight sclerosis in the basal arteries. On careful stripping of the pia mater the findings in the rhinencephalon were (the nomenclature in the following description has been adopted chiefly from Retzius [10]): —

Right Hemisphere. — The weight of the right hemisphere after hardening in formaldehyd was 604 gm. The bulbus and tractus olfactorius were absent. Corresponding to the area of the trigonum olfactorium a flat and small pyramidal pointed process could be seen; both its sides and tip were free, but the brain substance beneath adhered to its base. The tip of this process rested in a rudimentary sulcus olfactorius; no filia was to be seen. A rudimentary sulcus olfactorius ran forward from the top to the process described above for about 1.7 cm., and divided into two short transverse branches. As far as this sulcus extended a gyrus rectus could be distinguished, but at the end of the sulcus the gyri were bounded by a short transverse gyrus. Gyrus tuber olfactorius, gyrus olfactorius medialis and lateralis were not definite. Along the posterior ends of the gyrus rectus and gyri frontales a narrow convolution, a continuance of the area parolfactorici on the mesial surface, ran transversely into the limen insulæ and separated the surface connection between the frontal lobe and the anterior perforated substance. The space of the latter was narrow. No stria of olfactoria was to be seen. Sulcus parolfactorius anterior connected upward with the sulcus cinguli, and by the sulcus parolfactorius we could distinguish area parolfactoria and gyrus subcallosus, both pointing upward to gyrus cinguli (Fig. 2). The gyrus hippocampi was bounded anteriorly by incisura temporalis, above by the fissura rhinica in its anterior portion, and by sulcus collateralis on the posterior border; its length from the frontal tip to gyrus rhinencephalolingualis was about 4 cm. and seemed a little atrophied. From the inner sides of the hemisphere in which the crus cerebri was cut off could be seen clearly the whole length of the fascia dentate and the fimbria, and a part of the fornix through the dorsal surface of the gyrus hippocampi, with no pressing up of the thalamus. The

gyrus semilunaris, sulcus semiannularis, gyrus ambiens and sulcus rhinica inferior, which Retzius noted especially in the gyrus hippocampi, were easily identified. The uncus was well developed and bent sharply against the gyrus hippocampi as usual. The gyrus fusiformis was separated from the former gyrus by the fissura rhinica in its anterior portion, and posteriorly by sulcus collateralis, with the exception of a narrow communication, gyrus rhinencephalofusiformis, located between the former fissura and the latter sulcus.

At its posterior extremity the gyrus hippocampi joined with the gyrus cinguli by gyrus rhinencephalolingualis, with gyrus cinguli and also with the precuneus by the isthmus cinguli as well as by precuneus anterior. The sulcus cinguli as the continuation of the sulcus parolfactorius anterior at its frontal end ran upward then backward around the genu corporis callosi and joined with the sulcus paracentralis, which separated lobulus paracentralis and precuneus. The gyrus cinguli was well developed and separated from the neighboring gyri by sulcus cinguli and subparietalis, from the corpus callosum by sulcus corporis callosi. Its frontal end communicated with area parolfactoria and gyrus subcallosus; its posterior part was joined to the gyrus hippocampi. In the commisura anterior there was no notable change.

Left Hemisphere. — The weight of the left hemisphere after hardening in formaldehyd was 607 gm. The bulbus and tractus olfactorius were absent. In the place of the trigonum olfactorium there was a process of pyramidal form about the size of a kernel of corn, but it was not so flat as that of the right hemisphere; its tip was slightly free, but the other parts adhered to the frontal lobe beneath. Gyrus tuberis olfactorii, gyrus olfactorius medialis and lateralis could not be differentiated; neither could the filia nor the stria olfactoria. The gyrus rectus could not be differentiated from the gyri frontales, and a sulcus olfactorius did not exist. The space of substantia perforata anterior was narrowed and separated from the orbital surface by a sulcus which ran from the mesial surface as the continuation of sulcus parolfactorius posterior. The gyrus hippocampi was 5 cm. long from its frontal tip to the gyrus rhinencephalolingualis, and was bounded from the gyrus fusiformis by the sulcus collateralis. The fissura rhinica, gyrus semilunaris, sulcus semiannularis, gyrus ambiens and sulcus rhinica inferior could all be recognized. Generally the gyrus appeared to be a little atrophied, especially on the dorsal surface near the fissura hippocampi, where the con-

volution flattened, and clear strands of the fascia dentata, fimbria and a part of fornix were to be seen from the inner sides of the hemisphere (Fig. 3). The sulcus cinguli, beginning as the continuation of sulcus parolfactorius anterior at its frontal end, ran as usual almost parallel to the corpus callosum and combined posteriorly with the sulcus paracentralis. Gyrus cinguli, bounded superiorly by the sulcus cinguli and sulcus subparietalis, and below by the sulcus corporis callosi, was well developed, and its posterior end reached to the isthmus rhinencephalolingualis as usual. The anterior end of the gyrus cinguli joined below to the area parolfactoria and gyrus subcallosus, which were as well developed as those of the right hemisphere.

Histologic Study.

Although there is no definite proof of the location of the olfactory center in the human brain, it is not difficult to assume that either the gyrus hippocampi or the cornu ammonis may govern the function. Therefore I made it my chief object in the microscopic study to examine these two regions. I took out the whole gyrus hippocampi with the cornu ammonis and the fascia dentata from both hemispheres. I investigated the fine construction and the lamination of nerve cells by the cresyl violet stain in paraffin sections, the arrangement of nerve fibers by Kulschitzky-Wolter's modification of Weigert's myelinsheath stain in celloidin sections.

To obtain exact results I prepared as many serial sections as possible, and in order to avoid any misjudgment by comparison I investigated by the same methods the same regions of four other specimens which I had obtained from four normal looking hemispheres. I also examined other important areas of the brain.

Gyrus Hippocampi. — Cajal and Campbell have studied the normal histology of the gyrus hippocampi in detail. I state the findings in my case chiefly according to the topographical subdivisions by Ramón y Cajal, at the same time taking into consideration Campbell's description.

(*a*) The subiculum plexiform layer was about of normal thickness deep in this layer islets composed of numerous minute triangular cells were seen as usual. Four or five of them were found in a section of the frontal area, but much fewer in the posterior area. The pyramid and polymorphous cell layers were narrowed, and many nerve cells, especially the pyramidal cells, were moderately shrunken with more or less affected nuclei.

There was no change in the lamination, and the cells were arranged in regular parallel rows as usual. Glia cells seemed to be increased.

(*b*) Præsubiculum: The tangential fibers in the plexiform layer ran irregularly; some were swollen and pear-like in appearance. The thickness of the gray matter beneath was reduced, and many nerve cells, especially the pyramid cells, were moderately shrunken, but we were able to recognize the small pyramid and fusiform cell layer, the deep plexiform layer, the medium-sized and large pyramid cell layer, and the fusiform and triangular cell layer, as described by Cajal.

(*c*) The Hippocampal Gyrus Proper: The tangential fibers in the plexiform layer ran irregularly, and were much fewer than normal. In the layer containing a cluster of polymorphous cells, the clusters of large polymorphous cells which characterize this area of the gyrus were to be found at the lobulus pyriformis, less toward the posterior end, but their protoplasm as well as their nuclei were markedly shrunken. The deep plexiform layer or medium-sized pyramid cell layer, the large pyramid cell layer and the fusiform and triangular cell layer could all be differentiated, but many nerve cells, especially the pyramid cells, were considerably shrunken. As a whole, the cortex was narrowed. In Weigert's slides there was no notable change in the arrangement of the radial fibers in the gray matter, but the interradial fibers among the former were few in comparison with those in brains having olfactory tract intact.

Cornu Ammonis and Fascia Dentata. — The histology of these organs in the human brain has been studied carefully by Kölliker,[11] and Doinikow,[12] in his study of comparative anatomy, agrees with Kölliker.

(*a*) The Cornu Ammonis: The small size and the marked narrowing of the gray matter were noticeable at the first glance (Fig. 4). The microscopic investigation of the sections disclosed: the stratum zonale was about normal in thickness; the superficial tangential, middle longitudinal and deep tangential fibers could be differentiated. The glia cells were increased and the moderate thickening of the wall of the blood vessels was visible. The cell layer, stratum cellularum pyramidarium and stratum oriens were markedly narrowed as we recognized with the naked eye, and it was a striking fact that the pyramid cells which characterized this layer by their large size as well as by their number were not only much reduced and atrophied (Fig. 6), but in some

positions they had entirely disappeared, and these gaps of the cell layer were filled with neuroglia (Fig. 8). Many of the pyramid cells in this layer were also markedly shrunken; their Nissl's bodies could not be differentiated and their nuclei had disappeared. Such changes of the nerve cells could be seen through the whole cornu ammonis; generally they were more noticeable in its dorsal plate than in its ventral, and they were most striking in the terminal plate, as seen in Figs. 9 and 10. In the area near the gaps described the change of the pyramid cells was also remarkable, and in these situations the several stages of the cell alterations could be seen; some of them maintained their cell bodies only as a thread-like shell, while others kept their pyramid form with more or less affected protoplasm and nuclei. The favorite locations of the gap seemed to be the transitional regions of each plate into the other, and as far as I examined I found two spaces in the frontal part of the left cornu ammonis, and individual spaces in the frontal and in the middle part of the other.

In Weigert's stain not only could the narrowing of the layer of gray matter be seen clearly, but places in which the gray matter had almost disappeared and nerve fibers were pressed together as if they connected the stratum zonale with the alveus crosswise could be seen (Figs. 4 and 13).

The Alveus: This was about normal in thickness or thicker than normal along the dorsal plate; it divided into two branches as usual — the superficial branch went into the fimbria without notable alteration, but the nerve fibers of the deep branch which spread among the nerve cells in the terminal plate of the cornu ammonis were few and fine in comparison with those of the normal sections (Figs. 15 and 16).

(*b*) The Fascia Dentata and the Fimbria: In the stratum zonale nothing important was found.

Stratum Granulosum and Stratum Polymorpheus: The form and fine construction of each cell, as well as the number in a row, were about normal except in one area in which the ventral portions approached the surface; in this lesion many of the cells were moderately shrunken with alteration in their nuclei.

The Fimbria: There was no noticeable change in the fimbria, except that there were many blood vessels with thickened walls among the bundles of nerve fibers.

Other areas of the brain investigated were: the gyrus cinguli, gyrus temporalis superior, gyrus frontalis superior, gyrus centralis anterior, gyrus centralis posterior and gyrus occipitalis superior.

Speaking generally, the changes which I recognized in these areas, so far as I examined them, were the moderate thickening of the plexiform layer, more or less shrinkage of nerve cells in the gray matter, and light thickening of the wall of the blood vessels.

Summary.

There were bilateral absence of the bulbus and tractus olfactorius, rudimentary development of the trigonum olfactorium in both hemispheres, absence (left) and partial development (right) of the sulcus olfactorius, non-development of the gyrus olfactorius medialis and lateralis as well as of the gyrus tuberi olfactori in both sides, absence of the stria olfactoria, and some atrophy of the gyrus hippocampi in both hemispheres. The other areas, which are regarded as the rhinencephalon, showed no notable alteration.

Comparing this case with that of Weidenreich's, I find that there is no great difference between the two cases except in the incomplete development of the sulcus olfactorius and the atrophy of the gyrus hippocampi in my case.

As already mentioned, Weidenreich is of the opinion that, although the question of the olfactory center has not been solved by his case report, because no macroscopic change was to be seen in the rhinencephalon, perhaps the olfactory nerves connected the center in some irregular way, as the patient seemed to have had some sense of smell during life.

In my case the absence of the gyrus olfactorius medialis and lateralis, as well as of the gyrus tuberis olfactorii and the stria olfactoria, — which were also lacking in Weidenreich's Case, — would not be of importance in regard to the question of the olfactory center because the development of these gyri and stria depends directly on that of the bulbus and tractus olfactorius.

The flattened gyrus hippocampi, which I have described, attracted my attention in this case, and it would be interesting to know whether this atrophy in the rhinencephalon is to be regarded as the result of the absence of the lobus olfactorius. It is to be regretted that I could not get any positive information about the sense of smell of the patient during life. Such an important question could not be solved by the macroscopic investigation alone, and therefore I discuss it later in reference to the microscopic findings.

Concerning the origin of the defect of the olfactory lobe, according to the description by Ernst,[13] arhinencephaly, a brain without

an olfactory lobe, may develop when some compression acts on the head fold of the embryo. Schwalbe [14] states that the theory of compression as the cause of arhinencephaly and cyclopy has been shaken, and the opinion that it is due to some embryonal defect is gaining more general acceptance.

Weidenreich is of the opinion that in his case the olfactory nerve could not combine with the olfactory lobe as usual, and consequently the latter was deserted to atrophy. The full development of the sulcus olfactorius in his case shows that the olfactory lobe might have been developing for some time. He seeks the origin of the anomaly in some alteration of the embryonal connective tissue.

In the present case the sulcus olfactorius did not develop so fully, but, in accord with Weidenreich's, the main anomaly has been limited to the lobus olfactorius with no remarkable change in the neighboring areas of the forebrain. This is not to be explained by the compression theory, for if so, it must have been circumscribed as well as effective, and at the same time it must have acted on both hemispheres; but such a compression is not to be considered. I would not hesitate to believe that the defect of the lobus olfactorius might have had its origin in some defect in the embryonal tissue.

In the microscopic investigation the changes were found in the cornu ammonis. There were marked reduction in the gray matter, remarkable atrophy of pyramid cells and disappearance of the cell layer in some portions, fewer nerve fibers in the deep branch of the alveus, more or less increase of glia cells and thickenings in the walls of the blood vessels.

I believe that the change of the nerve cell denoted atrophy and not aplasia because the alteration was not the same through the whole cornu ammonis, and, moreover, several stages of the change in the cells were seen.

Next to the cornu ammonis the change in the gyrus hippocampi was most noticeable. The changes in this region were: less tangential fibers in the plexiform layer, marked atrophy of the superficial large polymorphic cells, moderate shrinkage of the pyramid cells and loss of the interradial nerve fibers.

It is interesting that to some extent these findings in the gyrus hippocampi accord with the result of the macroscopic investigation, which showed some atrophy of this gyrus. Moreover, it is extremely interesting to have found the most marked change in the cornu ammonis in my case, while the location of the

olfactory center is still a question, and some authors, notably Ramón y Cajal, are suggesting the cornu ammonis as the terminal station of this sense.

According to His, quoted in Weidenreich's paper, the olfactory nerve develops separately from its central part, and the connection with the brain is accomplished in a comparatively later stage. Therefore, it would not be unreasonable to expect some secondary change in the olfactory center, although it might have developed as usual. In this case, in which there were no bulbus and tractus olfactorius, the cornu ammonis showed the most marked alteration in the so-called rhinencephalon.

Besides the anomaly of the olfactory lobe are there any other possible causes for this change to be considered?

Arteriosclerosis may be taken into consideration, as the thickening of the walls of the blood vessels was noted in the cornu ammonis; but the patient did not have marked arteriosclerosis, and the basal arteries showed only a slight degree of the hardening. Hence an intense alteration in nervous tissue could not be explained by arteriosclerosis; moreover, the change in the nervous tissue was almost limited to the cornu ammonis.

Certain intoxications may be considered, but in the clinical history there is no evidence of any kind of intoxication as a probable cause of such a change in the nervous tissue. General intoxication would not cause the most marked change in the cornu ammonis; hence this cause may also be excluded. May I then conclude that I have eliminated doubt regarding the olfactory center, and that the cornu ammonis must be regarded as the terminal olfactory center?

Unfortunately, the patient suffered from epilepsy of long duration, as briefly described in the history. Since the sclerosis of the cornu ammonis in epilepsy was called to attention by Meynert, Sommer,[15] Bratz,[16] Arzheimer,[17] Worcester[18] and Southard[19] by histologic studies on this subject, I shall not give the results of the investigations of each one of these authors. It seems to be true that in several cases of epilepsy discussed by these physicians, some alterations — especially atrophy of pyramid cells, increase of glia cells and sclerosis of blood vessels — were found in the cornu ammonis. This complicates the value of similar findings in the present case, as the defect of the lobus olfactorius cannot be excluded as a possible cause of these changes in the cornu ammonis. A discussion as to which of the two possible causes is more reasonable or was more effective in

this case should be avoided, as any conclusion in this discussion appears to be only an assumption.

Although it is regrettable that this case could not bring out the soundest evidence necessary to solve the question of the olfactory center, I believe such a case and such an alteration in the cornu ammonis is a matter of enough interest to be reported, and may be a contribution to further investigation on this question.

In closing this report I wish to acknowledge my great indebtedness to Dr. E. E. Southard and Dr. M. M. Canavan, whose kind help enabled me to investigate the brain discussed. I also wish to thank Mr. Herbert W. Taylor, the photographer, who prepared the photographs.

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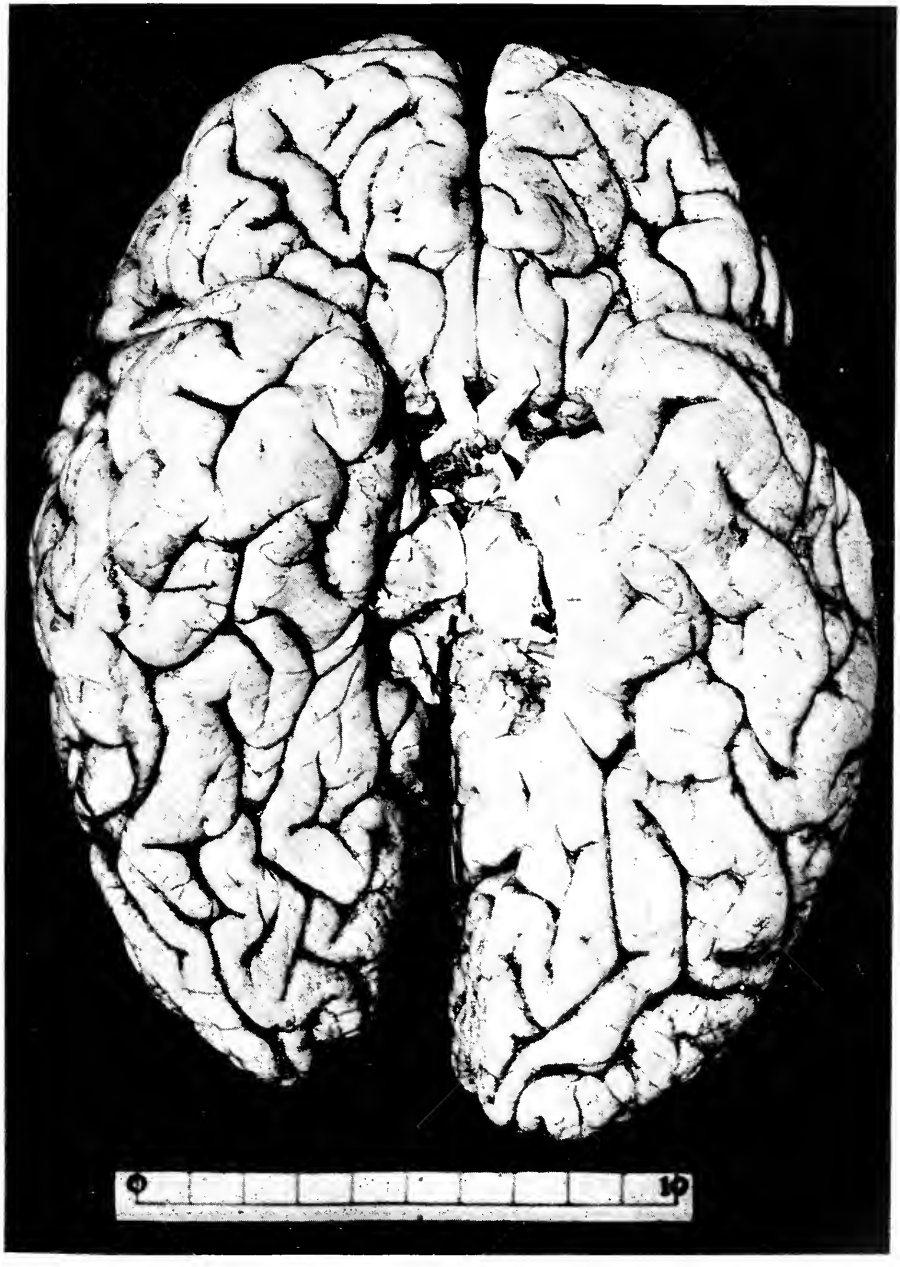


FIG. 1. —The base of the brain entirely bereft of bulbus and tractus olfactorius; rudimentary development of trigonum olfactorium and sulcus olfactorius are noticeable.

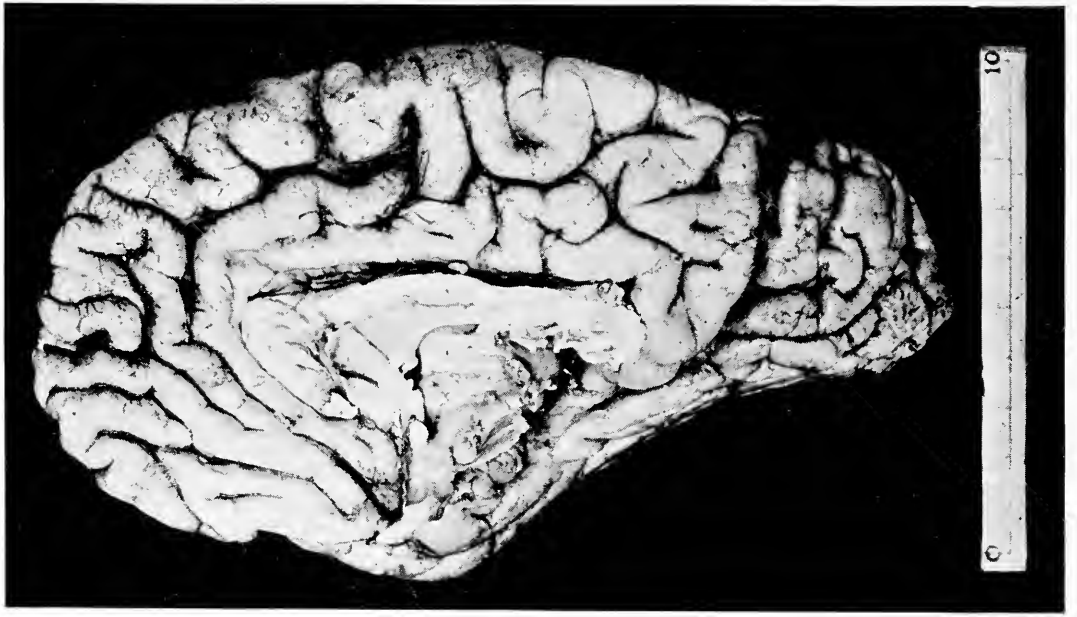


FIG. 2. — Mesial view of right hemisphere of the brain (see the description of macroscopic findings).

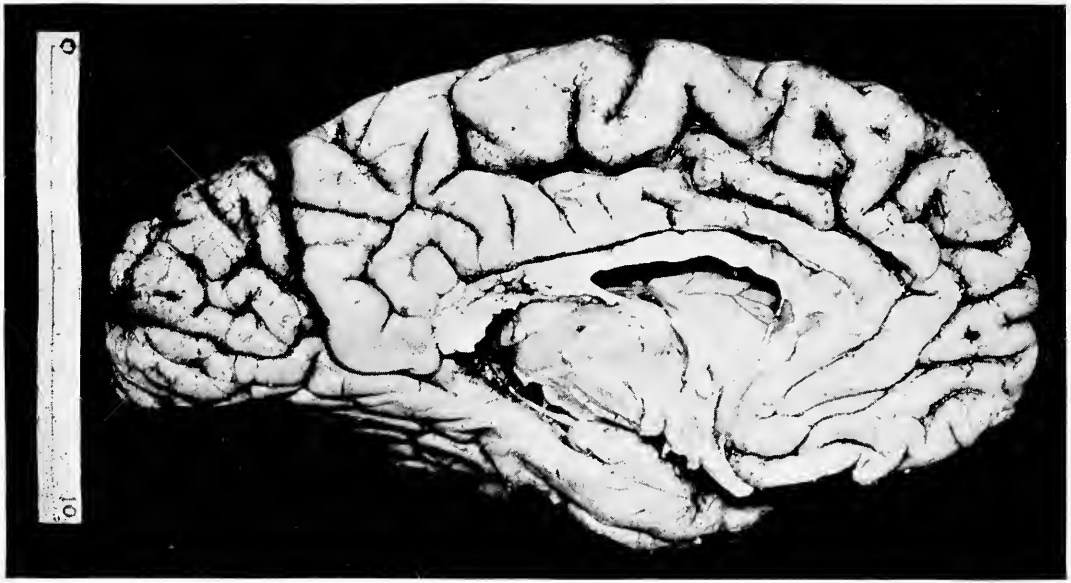
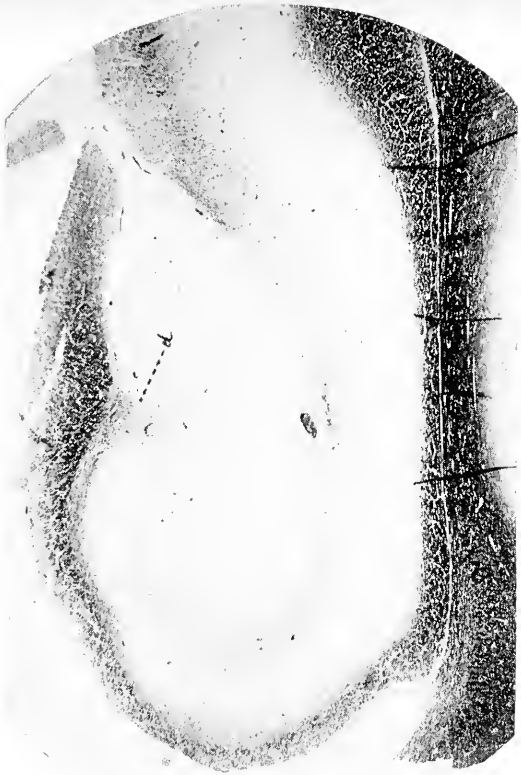


FIG. 3. — Mesial view of left hemisphere of the brain.



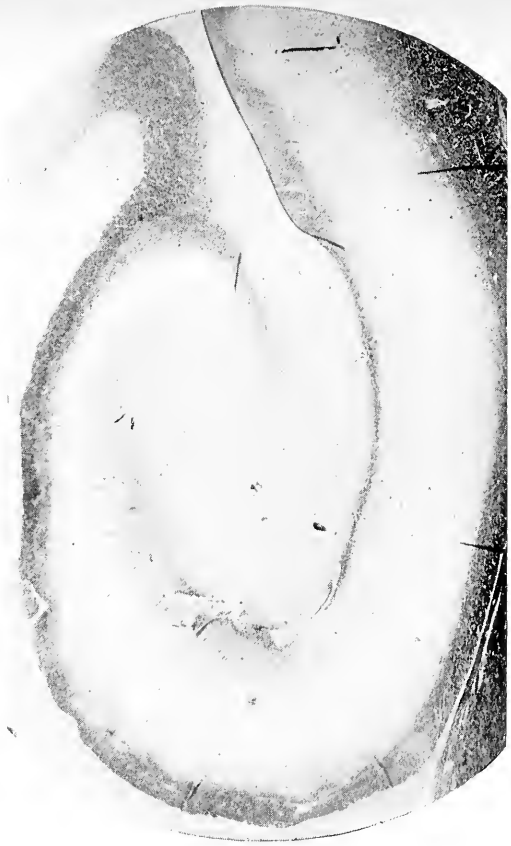


Fig. 4. Fig. 5.

Fig. 4. — Section of the cornu ammonis (right), which is atrophied and the layer of gray matter remarkably narrowed. The deep branch of the alveus (*d*) which spreads into the terminal plate (into fascia dentate) is shortened and stains poorly (see also Fig. 15). Compare this with Fig. 5.

Fig. 5. — Section of about the same region of a normal cornu ammonis. Kulschitzky-Wolter's modification of Weigert's myelin sheath stain; thickness, 15 microns.

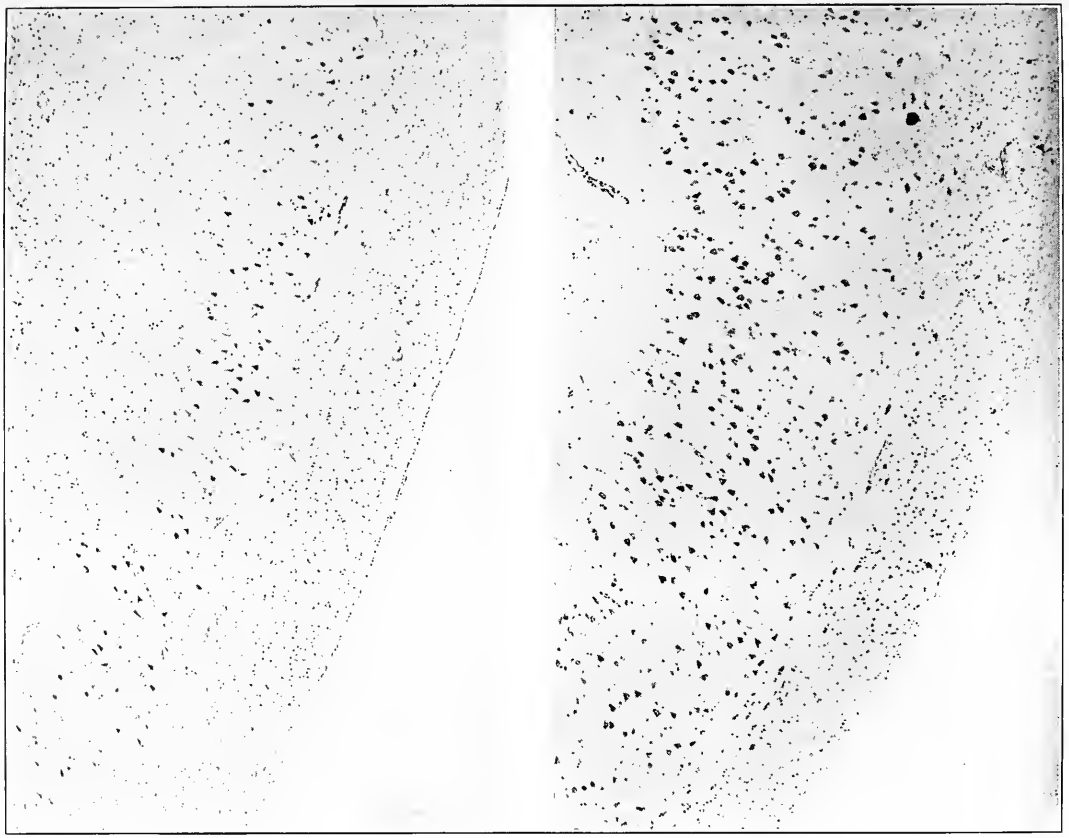


FIG. 6. FIG. 7.

FIG. 6. — An area in the dorsal plate of a section of the cornu ammonis (left); cell layer is remarkably narrowed, pyramid cells are reduced in number and atrophied; thickened walls of blood vessels are also noticeable. Compare this with Fig. 7.

FIG. 7. — The same area as in Fig. 6 of about the same region of a normal cornu ammonis. (Cresyl violet stain in paraffin section after formaldehyde and alcohol fixation; thickness, 6 microns.)

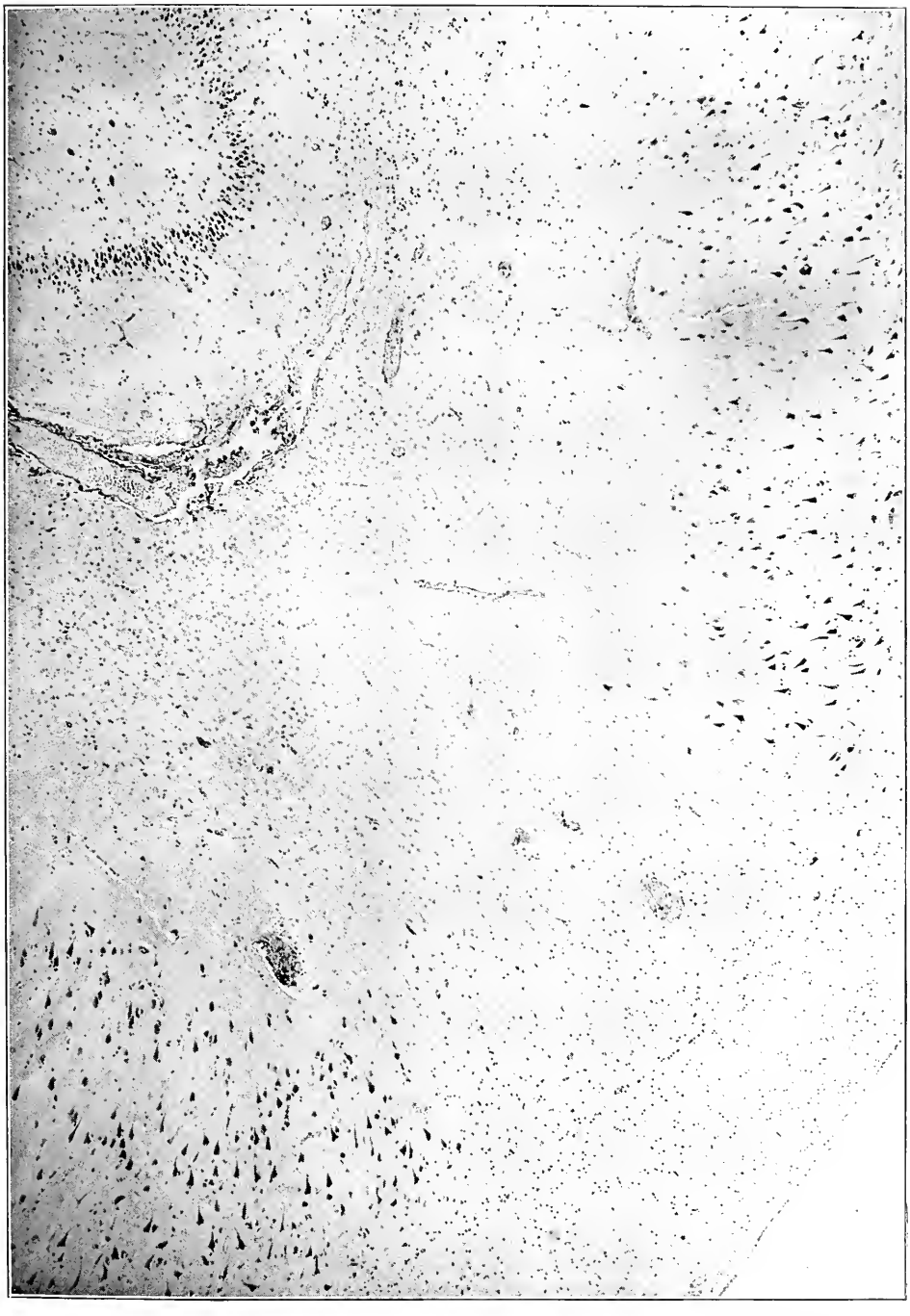


FIG. 8. — A gross gap of cell layer in the cornu ammonis (left). The pyramid cells have entirely disappeared in this lesion, and it is filled up by neuroglia. Atrophy of pyramid cells is also noticeable. Formalin and alcohol fixation; cresyl violet stain; thickness, 6 microns.

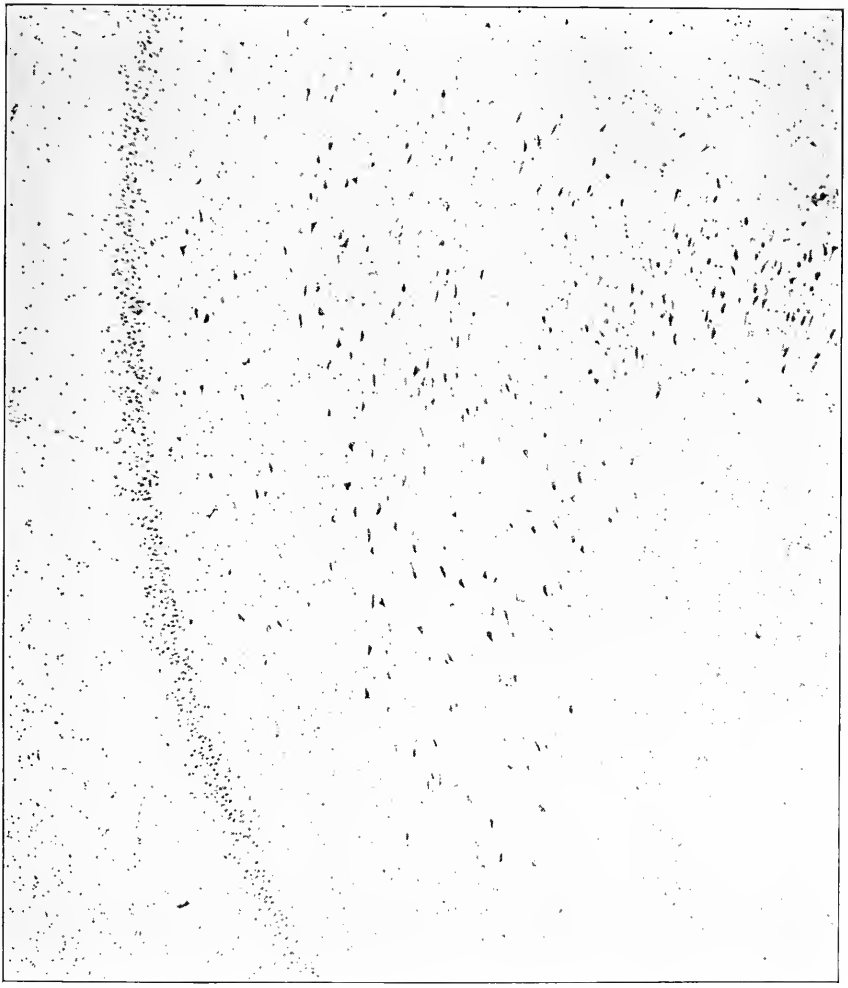


FIG. 9. — Alteration of nerve cells in the terminal plate of the cornu ammonis (left); they are reduced in number and markedly atrophied. Fine construction of these nerve cells can be seen in Fig. 10. Compare with Fig. 11.

FIG. 10. — Alteration of nerve cells in the terminal plate of the cornu ammonis (left); they are reduced in number and markedly atrophied. Fine construction of these nerve cells can be seen in Fig. 10. Compare with Fig. 12.

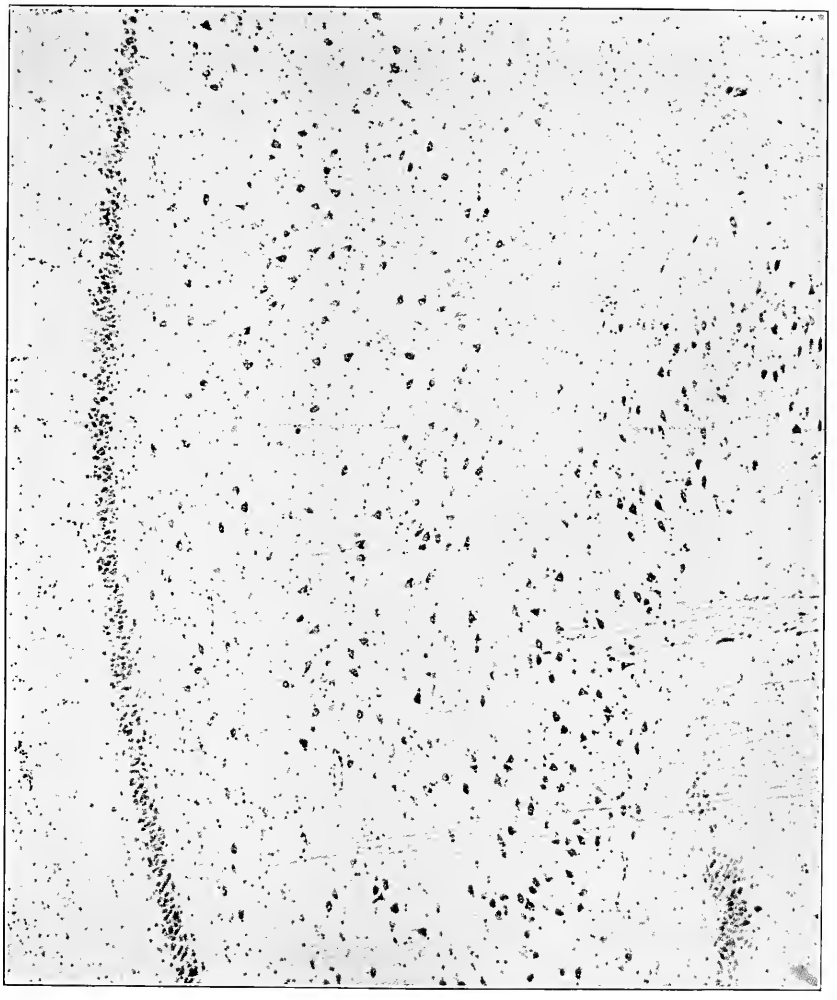


FIG. 11. — Nerve cells in the terminal plate of a normal cornu ammonis. Formaldehyde alcohol fixation; cresyl violet stain; thickness, 6 microns.

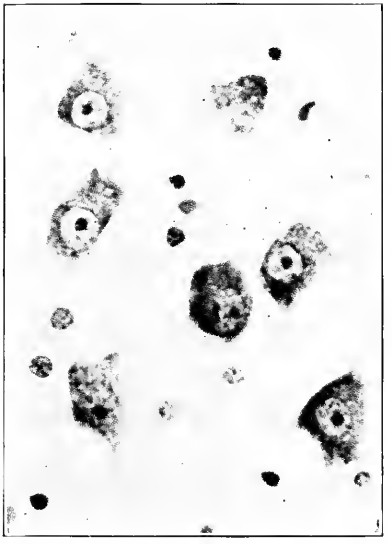


FIG. 12. — Finer details of these nerve cells shown in Fig. 11. Formaldehyde alcohol fixation cresyl violet stain; thickness, 6 microns.

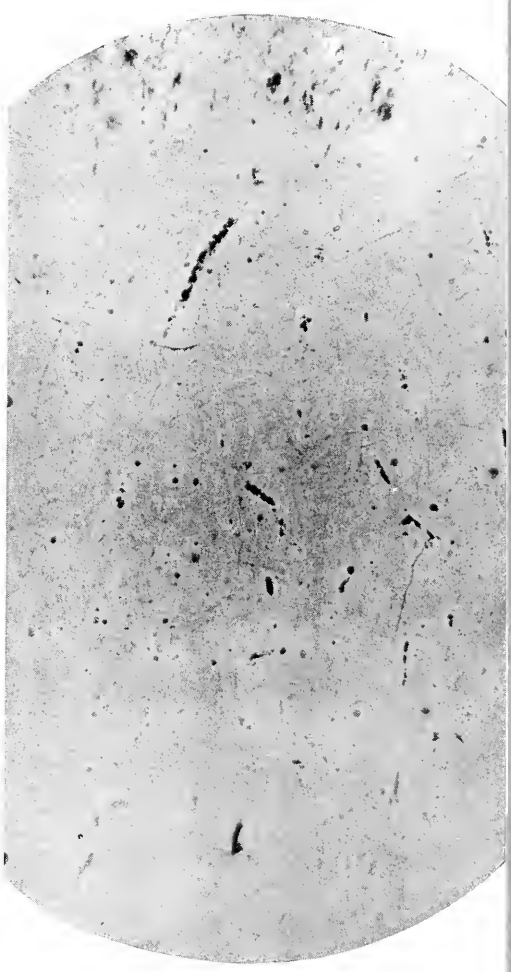


FIG. 13. FIG. 14.

FIG. 13. — An area in the dorsal plate of the cornu ammonis (right); in this lesion the gray matter has almost disappeared, and nerve fibers in the narrowed layer of gray matter are pressed together between stratum zonale (Z) and alveus (A). Compare this with Fig. 14.

FIG. 14. — The same area of about the same region of a normal cornu ammonis as in Fig. 13 (Z — stratum zonale). Kulschitzky-Wolter's modification of Weigert's myelin sheath stain; thickness, 15 microns.

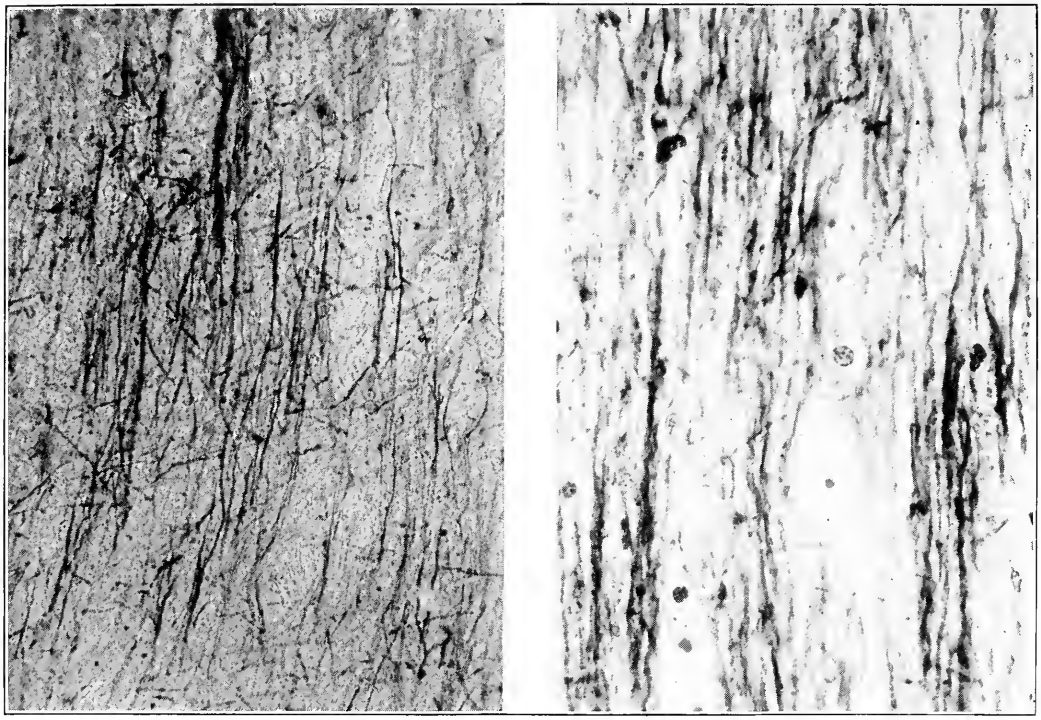


FIG. 15. FIG. 16.

FIG. 15. — Fine construction of nerve fibers in the deep branch of the alveus (see also Fig. 4). The area presents itself just before the deep branch spreads among nerve cells in the terminal plate of the cornu ammonis (right). The nerve fibers are reduced in number and atrophied. Compare this with Fig. 16.

FIG. 16. — Nerve fibers in the same area of about the same region of a normal cornu ammonis as in Fig. 15, Kulschitzky-Wolter's modification of Weigert's myelin sheath stain; thickness 15 microns.